96-TTT

ANIMAL CANCER RESEARCH ACT

HEARINGS

BEFORE THE

SUBCOMMITTEE ON DEPARTMENT INVESTIGATIONS, OVERSIGHT, AND RESEARCH

OF THE

COMMITTEE ON AGRICULTURE HOUSE OF REPRESENTATIVES

NINETY-SIXTH CONGRESS

SECOND SESSION

ON

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ANIMAL CANCER RESEARCH ACT

WEDNESDAY, AUGUST 20, 1980

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON DEPARTMENT INVESTIGATIONS,
OVERSIGHT, AND RESEARCH OF THE
COMMITTEE ON AGRICULTURE,
Washington, D.C.

The subcommittee met, pursuant to notice, at 10:02 a.m., in room 1302, Longworth House Office Building, Hon. E de la Garza (chairman of the subcommittee) presiding.

Present: Representatives Brown, Fithian, Skelton, and Wampler.

Staff present: J. Robert Franks, associate counsel; Glenda Temple, clerk; Bernard Brenner, Mario Costillo, Kathleen Garvin, and Gerald Jorgensen.

Mr. DE LAGARZA. The subcommittee will be in order.

The subcommittee meets this morning to hear testimony on S. 2043 as introduced by Senator Melcher, our distinguished former colleague of this committee.

The bill is to provide for research for the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife. The research would be conducted in appropriate facilities of the Department of Agriculture or by grants to other qualified veterinary research facilities.

The bill as passed by the Senate authorizes $25 million per year beginning in fiscal year 1981 for the USDA to conduct the research called for in cooperation with the Director of the National Institutes of Health.

[The bill, S. 2043, follows:]

II

96TH CONGRESS
1ST SESSION

S. 2043

To provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

IN THE SENATE OF THE UNITED STATES

NOVEMBER 26 (legislative day, NOVEMBER 15), 1979

Mr. MELCHER introduced the following bill; which was read twice and referred to the Committee on Agriculture, Nutrition, and Forestry

---

A BILL

To provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That this Act may be cited as the "Animal Cancer Research Act".

SEC. 2. Congress finds—

(a) that basic research on malignant tumors or cancers is essential to protect the health of domestic animals, poultry, and wildlife, including birds;

(b) that carcinogenic agents have not been adequately identified in domestic animals, poultry, and wildlife management;

(c) that basic research in diagnosis, prevention, and control of malignant tumors in animals and birds has not been adequately coordinated;

(d) that significant theories of a common factor in malignant tumors, such as chorionic gonadotropin, have not been pursued in depth; and

(e) that research on diagnosis, prevention, and control of cancer in animals and birds will be beneficial to identify any such common factors in both human and animal malignant tumors, if such exist.

SEC. 3. There is hereby authorized to be appropriated to the Science and Education Administration of the Department of Agriculture $1,500,000 for fiscal year 1980, $3,000,000 for fiscal year 1981, and $5,000,000 annually thereafter for the conduct of basic research on cancer in animals and birds at appropriate facilities within the Department of Agriculture or by grants to other qualified veterinary research facilities.

READEX FICHE

Mr. DE LA GARZA. We start this morning's hearing with Senator Melcher. Senator, we welcome you and are always happy to see you. We appreciate, as always, your continuing interest in this field. We would be very happy to hear from you at this time.

STATEMENT OF HON. JOHN MELCHER, U.S. SENATOR FROM THE STATE OF MONTANA

Senator MELCHER. Thank you, Mr. Chairman.

It is a real pleasure for me to be back in this room meeting with my old committee since I served on this committee when I was in the House of Representatives. There have been many times when I very much missed working on this committee which has been so fruitful and productive.

Mr. Chairman, the hearing you are holding today on the Animal Cancer Research Act demonstrates the concern of Congress that we make better use of Federal dollars earmarked for cancer research.

The importance of basic research on cancer in animals, with its potential benefit to research on human cancer, cannot be overemphasized. A $1 billion annual appropriation for cancer research assigns very little of that to basic research involving domestic animals and birds, which obviously share the same or similar environment with man. Clearly, basic cancer research for animal and man complements each other.

I introduced S. 2043, the Animal Cancer Research Act, on November 26, 1979. Just 2 weeks later, on December 10, there were hearings on the bill before the Senate Subcommittee on Agricultural Research and Investigations. On May 22, this year, the Senate approved the bill without dissenting vote.

As passed by the Senate, the bill authorizes $25 million per year beginning in fiscal year 1981 for the Department of Agriculture to conduct basic cancer research on birds and animals in cooperation with the Director of the National Institutes of Health.

The bill requires the Secretary and the Director to review annually the research program to coordinate with the National Cancer Institute.

While there is cooperation between scientists at NIH and their counterparts at USDA's Science and Education Administration, it is limited by a lack of funding available for the Department of Agriculture to use significant amounts for animal cancer research.

An outstanding breakthrough in poultry cancer control occurred in the early 1970's when a vaccine to control Marek's disease was developed as a result of Science and Education Administration Research.

Before the development and use of a vaccine, Marek's disease was a devastating threat to the poultry industry, with losses estimated in excess of $150 million annually in the United States.

Then, in 1969, Dr. Richard L. Witter, working at SEA's Poultry Research Laboratory in East Lansing, Mich., isolated herpes virus, and later that year Dr. Purchase demonstrated that it gave protection against Marek's disease.

In 1970 he conducted field trials on herpes virus to show it protected animals outside the laboratory. In November of that year, the vaccine was licensed for use in Michigan and in March

971 it was licensed by USDA's Animal and Plant Health Inspec-
on Service for national use.

The virus, which commonly occurs in turkeys, is injected into
ay-old chicks to protect against Marek's disease. SEA has done
is on a comparatively limited budget. I am convinced that an
crease in basic research work on cancer in animals and birds
ould definitely be granted. With additional funding, further ad-
ances can be made.

I fully recognize that NIH is not indifferent to research on
nimal cancer. The Division of Research Resources at NIH oper-
es primate research centers. At those centers, research is con-
ucted which takes advantage of those characteristics of nonhuman
rimates that are uniquely suited for biomedical research identifi-
ble with national needs.

Some of those studies have involved the cottontop marmoset, the
nly species of monkey known to mankind that is susceptible to a
irus thought to cause cancer in human beings. The work is laud-
ble, but it leaves behind some problems. Let me explain.

In the December hearings on S. 2043, one of the witnesses was
r. Myron Blume of the Mount Zion Hospital in San Francisco. He
ade this very telling observation:

> I think also examining in more depth the tumors that occur in farm animals, in
> mestic animals, pets, and wildlife is important. The animal models that are
> nventionally used in cancer research for the most part are susceptible to a variety
> induced tumors, induced by chemical or virus, or "spontaneous" tumors, which
> em to depend on the inbreeding of the animals for their expression.

I agree, Mr. Chairman. Scores of thousands of rats, mice, and
her animals, and some primates, constitute a substantial concen-
ation resources in our cancer research program. That concerns
e.

If we focus our efforts too much on animals that are bred—often
bred—to be born and to die of cancer, we may be squandering
e opportunity to investigate the many additional variables that
ay lead to cancer in animals and man living in the environment
utside of the research laboratories.

That reinforces the need, not only for an expanded animal
ancer research effort but also the need to explore further and
ore intensively cancer in our farm animals, our companion ani-
als, and birds.

NIH has done intensive work, but the results have not been as
roductive as we might have hoped. Much can be done to make
ancer research at NIH more innovative with fundamental ap-
roaches to basic research. A good example of that is the matter of
horionic gonadotropin.

Dr. Bob Netterburg—not a researcher himself but a dentist by
rofession—has consistently argued over the past several years
at recognition of some previous research on chorionic gonadotro-
in has been ignored by the National Cancer Institute, and that
ery little attention has been paid by NCI to grant applications by
esearchers in this and other areas. Dr. Netterburg has document-
d these facts in his recent publication, "The Road Not Taken:
oward a Cancer Vaccine."

S. 2043 was introduced to provide more emphasis through the
cience and Education Administration for basic research on cancer
n animals. Specifically, the bill directs emphasis on basic research

on common agents found in many types of cancer such as chorionic gonadotropin.

While the Science and Education Administration has an ongoing program of researching the physiology of chorionic gonadotropin, it has not attempted the research on the basis of its linkage as an agent with animal cancers. The bill specifically is intended to develop basic research on cancer in this area.

Whatever the attitude of the National Cancer Institute has been in the past to basic innovative research, we are beginning to take steps toward making sure that trail-blazing research proposals get a better hearing.

In June the Senate passed S. 988, the Health Sciences Promotion Act of 1980. One of its provisions encourages the evaluation of methods for selection of grants which could replace the current system of peer review study groups. Another provision would attempt to find ways to identify innovative and unconventional research and utilize the expertise of generalist scientists.

House approval of S. 2043 can help carry the effort further. Passage of the bill will bring together the work of the Science and Education Administration, which includes animal health research and the National Cancer Institute. It is high time we do this to break new ground in the war against cancer.

Commonsense tells us to research the obvious. What affects humans in the national environment of the 20th century affects animals and vice versa. This bill emphasises the basics. It authorizes a very small percentage—2.5 percent—of the $1 billion spent on cancer research annually to be used in more intense study of cancer in animals.

I strongly hope that these hearings will lead to full committee approval and quick action by the House of Representatives so that we might begin to use more effectively the work now being done with Federal funds and in separate units of government. We are not talking so much here about new money as we are talking about new opportunities. I hope we will grasp the chance while we have it.

Mr. Chairman, that concludes my testimony.

I would also like to submit to the committee some testimony of Dr. Vernon Stevens of the Ohio State University of Columbus, Ohio, on this bill.

He could not be here today, but he has a vital interest in it. I think it will make a good addition to the hearing record.

Dr. Stevens' work in this field has been outstanding. He is a strong supporter of the bill.

Mr. DE LA GARZA. Thank you very much, Senator.

Without objection, we will accept and include in the record the statement of Dr. Stevens.

[The prepared statement of Dr. Vernon C. Stevens follows:]

Dr. Vernon C. Stevens
The Ohio State University
Columbus, Ohio

Mr. Chairman and Members of the Subcommittee, I appreciate the opportunity to submit a statement on S. 2043 dealing with research on malignant tumors in domestic animals. I am a professor at Ohio State University with appointments in the Departments of Obstetrics and Gynecology, Pathology and Zoology. My field of specialization is reproductive biology. The remarks I would like to make regarding S. 2043 relate to 1) animal species used for investigating the cause and treatment of tumors, 2) limitations in scope of currently funded cancer research programs and 3) the importance of research related to chorionic gonadotropin for defining causes and treatment of malignancies.

The vast majority of research conducted on cancer is done with small laboratory animals, such as rodents, as tumor hosts. Costs and space requirements are factors in such selection although my personal experience is that studies in farm animals at Land Grant colleges are often little more expensive than studies in rabbits or guinea pigs in an urban research laboratory. Most important, the use of convenient, small laboratory species for the bulk of studies may be a serious oversight in studying causes of cancer in domestic animals or humans. Further, it is well known that defense mechanisms against tumors and responses to tumor therapy vary widely among species and more relevant data may be obtained more rapidly if more studies were conducted in domestic animal species. The importance of cancer to the production of food from farm animals has been related to the Subcommittee by others and it should be clear that if this source of animal wastage is to be reduced, the species effected should be used in the research studies.

Research funds from NIH and NCI are distributed to a relatively few scientists who have established themselves as competent investigators in the classical methods of cancer detection, therapy and/or testing the relative activity of carcinogens or anti-tumor agents. This field is like a bureaucracy with resistance to change or major shifts in emphasis of research programs. Government administrators, as well as scientists reviewing funding, tend to avoid any concept that will involve radical departures from standard procedures or persons who have not concerned themselves for many years with cancer research. This posture is detrimental to vigorous, creative inovations in the search for solutions to the diagnosis and treatment of cancer in animals or humans. There are hundreds of excellent scientists in this country in veterinary schools and animal experimental stations with the background and

interest in pursuing cancer research. To virtually ignore this block of talent in distributing the cancer research funds from the major funding agencies represents, in my opinion, poor management.

The third area I wish to discuss, the importance of chorionic gonadotropin (CG) in cancer research, is one that I am most concerned about and represents a feature of S. 2043 that motivates me highly to support it. First of all, let me be somewhat immodest and state that I know quite a bit about CG. I have been involved with studies of CG in relation to human fertility for more that 17 years. Our laboratory has developed a vaccine for controlling fertility based on immunity against CG and the testing of its safety is now underway before applying it to human populations. During the research on this vaccine, I have become familiar with the work of others in relating the association of this hormone to tumor cells and the presence of it in the blood of cancer patients. I have supplied antisera and other reagents to many scientists pursuing research to relate the reasons of this CG-tumor association. My research, showing CG being essential to prevent the mother's rejection of pregnancy, has revealed striking similarities between self-preservation of pregnancy tissues and the self-protective features of tumor cells. Precisely how CG is involved in this protection is not now known, however, the abundance of data available to implicate this substance in tumor survival makes it difficult to imagine why a major research effort by the cancer funding agencies is not underway to explore this promising lead.

To the best of my knowledge, no major research grant has been awarded by NIH, NCI or by the Science and Education Administration, Department of Agriculture to specifically support CG research in relation to the diagnosis or treatment of cancer. I do know that some of my colleagues, outside of the Cancer Research Establishment, have tried unsuccessfully to obtain research monies from NIH and NCI for this purpose. One could always argue that each proposal is evaluated on its individual merit and that these attempts were rejected due to poor proposal preparation or lack of credentials by the scientist involved. However, should this have been the case, one can ask why were not other more acceptable scientists sought out by these agencies to conduct the needed studies.

The Bill S. 2043 is a step in the right direction to rectify serious ommissions in all three of the areas discussed above. I urge the Subcommittee to give their full endorsement.

Mr. DE LA GARZA. Are there any questions?

Mr. WAMPLER. Mr. Chairman, I have a brief statement. I understand there is a rollcall under way in just about a minute.

Mr. DE LA GARZA. The gentleman is recognized.

REMARKS OF HON. WILLIAM C. WAMPLER, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF VIRGINIA

Mr. WAMPLER. Thank you, Mr. Chairman.

I would like to take this opportunity to welcome our former committee colleague, Senator Melcher, and to commend him for his initiative in introducing this legislation, S. 2043, the Animal Cancer Research Act.

I am hopeful that we will be able to mark up this legislation at an early date and I want to state for the record that I support the thrust of this legislation.

For many years I have been a firm believer in agriculture research, feeling that it is beneficial to the producer as well as the consumer. The amount of money that this Nation spends for research is returned manyfold by the fruits of such endeavors.

This committee evidenced its interest in animal research most recently when it included title XIV in Public Law 95-112, the Food and Agriculture Act of 1977. Subtitle E—Animal Health and Disease Research—was designed primarily to improve the health and productivity of our domestic animals and poultry.

In that subtitle we particularly specified that colleges of veterinary medicine qualified for research funding, and I am assuming that such institutions will be considered as eligible for such funding under this legislation.

If there is any question about that, we should give consideration to clarifying the intent of Congress as it relates to this issue.

It would be my observation that basic cancer research on animals and man should not be mutually exclusive. In developing a vaccine for poultry cancer we cut the losses to the poultry industry dramatically, and hopefully that research will be used not only for further animal cancer studies but for human cancer research as well.

It is reasonable to expect that animal cancer research can be helpful in research involving the causes, prevention, and possible cure of forms of cancer in human beings. In seeking a cure for human cancer we should leave no stone unturned.

The assistance that we receive from animal research should be double-edged, cutting two ways, helping both animal and man. Section 4 of the bill, calling for review of the research conducted under this bill to be coordinated by the Secretary of Agriculture with the Director of the National Institutes of Health, recognizes this important dual benefit.

Mr. Chairman, I appreciate your scheduling this hearing and I look forward to the testimony of these witnesses.

Thank you.

Senator MELCHER. Thank you very much.

Mr. FITHIAN. I have questions, Mr. Chairman. I am not sure we have time for them.

I welcome Senator Melcher back to the committee.

In your statement, on pages 3 and 4, there is an indication that you believe the side effect of the research on animal cancer may well be applicable to certain findings with regard to the human cancer research as well. Do I read that correctly?

Senator MELCHER. Absolutely. If there are any common links, such as chorionic gonadotropin, I am sure we will find them.

Mr. FITHIAN. The second question I am not clear on is this. First, let me say I am very supportive of your work and commend you for introducing the bill. We will obviously work for its passage.

Do you visualize any of this to be dedicated to the question which we in agriculture frequently have to face, the transfer of cancer-producing elements from animals to humans in the course of eating meat?

Senator MELCHER. The opportunity is there. I will not venture into that because I think what we are trying to do here is basic research. We had better leave to the scientists the avenues they want to follow in basic research.

It is absolutely geared for basic research. They may find that indeed they do want to look at aspects where chemicals that both man and animals are susceptible to might have some common link. Animals are susceptible to it and perhaps humans are also.

I think we have gone too far down the road just looking at rats, mice, and guinea pigs in the laboratory. It is time we back off from that and look at animals that share our environment, not the laboratory environment.

Mr. FITHIAN. Thank you.

Mr. DE LA GARZA. Thank you very much, Senator. We appreciate your being here.

Senator MELCHER. Thank you.

Mr. DE LA GARZA. There is a rollcall in the House. We are going to recess in order to make that rollcall, then we will hear our second witness.

[Recess taken.]

Mr. DE LA GARZA. The subcommittee will be in order.

The next witness is Dr. Terry B. Kinney, Jr., Administrator, Agricultural Research, Science and Education Administration, U.S. Department of Agriculture.

We will be happy to hear from you at this time.

STATEMENT OF DR. TERRY B. KINNEY, JR., ADMINISTRATOR, SCIENCE AND EDUCATION ADMINISTRATION, AGRICULTURAL RESEARCH, U.S. DEPARTMENT OF AGRICULTURE, ACCOMPANIED BY JOHN VICTOR, CHIEF, BUDGET DIVISION, AND DR. EARL J. SPLITTER, ACTING DEPUTY ADMINISTRATOR, SCIENCE AND EDUCATION ADMINISTRATION, U.S. DEPARTMENT OF AGRICULTURE

Dr. KINNEY. Thank you, Mr. Chairman.

Mr. Chairman and members of the subcommittee, thank you for the opportunity to testify on S. 2043, the Animal Cancer Research Act, and the research on malignant tumors which the Science and Education Administration is conducting in animals.

I am accompanied by John Victor, Chief, Budget Division, SEA; and Dr. Earl J. Splitter, doctor of veterinary medicine, and Acting

ty Administrator, Science and Education Administration, Co-
ative Research Service.
e Department supports the intent of this legislation. However,
Department has adequate authorization and funding for this
rch, and does not believe that enactment of S. 2043 is neces-
The Department does recognize that some aspects of cancer
rch could possibly be more intensively reviewed. However, we
not prepared to ask for additional authorization at this time.
sses in livestock and poultry caused by malignancies have
of continuing concern to the Department. In 1978, tumerous
itions resulted in the loss of millions of pounds of federally
ected meat animals and poultry because of condemnations at
of slaughter. This does not include the very substantial but
easured losses due to reduced productivity and deaths occur-
from malignancies in animals on the farm.
tensive research efforts by the Science and Education Adminis-
on and its cooperators in the past decade have led to major
kthroughs in controlling several of the most important causes
alignancies in farm animals. Cancer viruses and cancer cells
been grown artificially in culture and their chemical and
genic makeup determined. Mechanisms of virus and cell repli-
on have been studied and compared with replication of other
ses and normal cells. From these discoveries the mechanism of
smission has been better understood and diagnostic tests have
developed.
arek's disease of poultry, a leukemia-like malignancy, has been
d to be caused by a virus. This discovery led to the develop-
t of a vaccine which has resulted in annual losses from the
ase formerly at $200 million being reduced now to about $30
ion. The mechanism of the protection has been shown to be
iated by both cellular and humoral responses against new anti-
that are characteristic of and appear in tumor cells. Leukemia
attle also has been found to be of viral origin, and technology
been developed which will lead to reduction and perhaps even
elimination of the disease. SEA research also has determined
cause and provided means for controlling the malignancy-like
ase of mink known as Aleutian disease. This was a major cause
sses in the production of mink for fur.
espite these advances, other formidable malignancy problems of
stock and poultry remain to be solved. SEA currently—fiscal
1980—is allocating $8.3 million for this research.
he Science and Education Administration, in cooperation with
er Federal agencies and other institutions, has a significant
gram in basic research on cancer in animals. This includes
lies on the genetics of the immune response, possible causative
nts of different kinds of cancer, the effects of these agents on
host genetic materials that change in the process of becoming
cerous, mechanisms by which the control of cell proliferation of
cerous cells is lost, and methods to identify new antigens, recep-
, and other substances on the surface of cancer cells.
ther efforts by SEA and its cooperators to solve animal malig-
cies include studies to prevent cancer-eye in cattle and pulmo-
y adenomatosis in sheep. More effective methods are being
ght to reduce or eliminate leukemia of cattle and Marek's dis-

ease and lymphoid leukosis of poultry. In addition, studies are in progress on mechanisms occurring in animals that affect natural and acquired immunity to malignancies. Promising substances are being evaluated that show suppressant action against the multiplication of animal tumor cells.

Another major effort is centering on the problem of mycotoxins, a group of probable carcinogens for man and known carcinogens and toxicants for animals. Methods are being sought to reduce or eliminate if possible these carcinogens from food and feeds. A portion of the basic research program on mycotoxins is related to cancer in animals including the effect of mycotoxins on the cellular and humoral immune response, the ability of animals to resist disease, the ability of animals to respond to vaccines and the effects of mycotoxins on cellular genetic components that result in cancer.

SEA has a strong program on cancer in animals and basic research on animal reproduction. These programs give high priority to solving problems of significant economic importance in farm animals. We are not proposing to reduce any of these high priority programs.

SEA has ongoing programs on the mechanisms of reproduction involving pituitary and gonadal hormones. Chorionic gonadotrophin causes ovulation as does the pituitary luteinizing hormone which is important in farm animals. Chorionic gonadotrophin is used extensively in research as a tool, often in combination with other hormones, to regulate ovarian function.

Some of the research problems are in the clarification of the nature of the hormone chorionic gonadotrophin and the mechanisms of its action including its role in stimulation of cell proliferation and its possible role in the acceptance or rejection by the animal of embryo cells or cancer cells.

We agree with statements in S. 2043 that basic research on malignant tumors is essential to the health of animals; that such research may be beneficial in determining whether there are common factors which may cause malignancies in both man and animals; and that all carcinogenic agents have not been adequately identified in domestic animals.

We believe there have been and continue to be well-coordinated efforts to solve the malignancies of food animals which cause major economic losses. The health-related research programs of SEA are regularly reviewed and adjusted as necessary to assure that attention is being directed to the most important problems. The successes just referred to in this testimony in controlling Marek's disease in poultry and in solving the cause of leukemia in cattle did not result from isolated studies, but were due to well-coordinated efforts by SEA and its cooperators. These efforts resulted in advances of substantial significance to veterinary as well as medical science. This included the first cancerous disease for which a successful, commercially applicable vaccine was ever developed and the vaccine is now applied worldwide. Another major advance included conclusive proof of the viral cause of leukemia in cattle—a question not completely resolved as yet in the similar disease of human leukemia.

In conclusion, we believe that current authorizations are adequate for continued, productive studies by SEA on malignancies of food animals. Currently, $8.3 million of the $68.9 million of SEA's fiscal year 1980 appropriation for animal protection research—or about 12 percent of that money—is being spent on malignancy research. We would expect to be spending at least the same amount in fiscal year 1981. Given the basic nature of the research involved, research is being conducted in other Federal agencies directed toward these same underlying factors.

Mr. Chairman, thank you very much for the opportunity to testify before your subcommittee. My colleagues and I will be glad to answer your questions.

Mr. DE LA GARZA. Thank you very much, Dr. Kinney.

Mr. BROWN. I have no questions.

Mr. DE LA GARZA. Mr. Wampler?

Mr. WAMPLER. Thank you, Mr. Chairman.

Dr. Kinney, I want to thank you and your associates for appearing here this morning and sharing the testimony with the committee.

I commend you for your statement on page 1 that the Department supports the intent of this legislation. Quite frankly, I wish you were a little more enthusiastic and say you support not only the intent but the legislation itself. I think it is legislation that is long past due.

I want to ask you, as you have read the bill and as you understand it, is there anything in the bill, assuming it becomes law, that would preclude or prevent a school of veterinary medicine from participating in any research grants or studies that might be made?

Dr. KINNEY. No, I do not interpret the bill to exclude any veterinary school from participating. In fact, in much of our research relating to cancer in animals, we have cooperated with schools of veterinary medicine. We do recognize them as extremely important.

Mr. WAMPLER. I think they have a good record in that regard. It is my feeling that in schools of veterinary medicine throughout the country we have extraordinarily large expertise of information and facilities that could be utilized in a cooperative effort with other research that is being done in-house and others that you choose to carry out the research.

I am concerned that I have observed through the years, and it is perhaps truer in the old Department of HEW, that research funds were being allocated to carry out various types of research on cancer and the panels that reviewed the grant applications frequently do not have veterinarians serving on these panels.

People who have no expertise or knowledge of veterinary medicine served on these panels. In many cases I think research in the fields of diseases of animals and also perhaps investigations and studies into cancer have been neglected.

I realize this is not your area of administration but I just want to point it out. It seems to me that veterinarians and veterinary schools have been largely overlooked in this process.

Last evening I had the opportunity to review the book that Senator Melcher referred to. It is by Dr. Netterburg, a dentist. I do

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not necessarily agree with the conclusion, but it is a rather strong indictment.

It says, among other things, that the directive research and other activities of the National Cancer Institute and of the American Cancer Society have been scandalously counterproductive in the conquest of cancer.

Obviously Dr. Netterburg feels very strongly. I hope that regardless of whether S. 2043 becomes law or not that SEA will continue in an aggressive way to see that there is coordination between the National Institutes of Health and the ongoing programs in the Department of Agriculture and that there is better coordination or the best coordination possible considering the resources that you have to work with.

The thing that is of concern to me is that now only about 2 percent of the total budget for research and development of the Federal Government goes to Agriculture.

This type of research truly comes under that classification. At one time I think Agriculture enjoyed as much as one-third of the total research budget of all the agencies of the Federal Government. But through the years we have seen that depressed.

You indicated in your statement that you feel that the present authorization you have will permit you to proceed in an orderly fashion to better coordinate your efforts with NIH and other agencies of the Government.

I just want to commend you and encourage you to continue to do the good job that you are doing. Obviously I think you can point with pride to what has been done. But I do not think we really have achieved our ultimate maximum effort by any means. I hope this Congress will respect in a more meaningful way and give you more resources with which to work.

Again, I appreciate your being here. If this bill were to pass the House of Representatives and be presented to the President for signature, I hope the Department indeed would give a favorable report and urge the President to sign it into law.

Thank you.

Dr. KINNEY. I would like to simply comment that I think our respect for the capabilities of veterinarians as researchers, is reflected in the fact that the developers of the vaccine for Marek's disease are now continuing to work on that and are working on avian leukosis—many are veterinarians.

The group at the National Research Center at Ames, Iowa, are almost all veterinarians or DVM's. So, we who do not have a DVM have to acknowledge that our DVM's are outstanding researchers indeed. We fully support the concept of cooperative work with veterinary schools.

Mr. WAMPLER. I did not mean to criticize the Department of Agriculture or other agencies. Other agencies, especially HEW, did not always recognize that.

Dr. KINNEY. I wanted to assure my colleagues in attendance who have veterinary backgrounds that we are very much aware of their capabilities and we intend to capitalize on that as much as possible.

Mr. WAMPLER. I commend you for that. Thank you very much.

Mr. DE LA GARZA. Mr. Skelton?

Mr. SKELTON. Dr. Kinney, I notice in your conclusion that you believe that current authorizations are adequate. You point to the fact that over $8 million, or 12 percent, of last year's money was allocated to animal cancer-type research. Is that correct?

Dr. KINNEY. Yes.

Mr. SKELTON. In other words, you are saying that what you have done in the past and what you expect to do in fiscal year 1981 is adequate and you do not need any more money. Is that what you are telling us?

Dr. KINNEY. The statement indicates that the current authorizations——

Mr. SKELTON. Forget the statement. Tell me what you think.

Dr. KINNEY. I think within the capabilities that we have for research now, looking at all of our research on animal protection or animal diseases, yes, I think we have adequate funds for research on malignancies in animals.

Mr. SKELTON. In other words, you would be opposed to this bill in its present form, this Senate bill?

Dr. KINNEY. No. I think in my statement I indicate that we would support the intent of the bill. But we would not solicit additional support for research on malignancies.

Mr. SKELTON. If it is an authorization bill and the authorization passed, of course that is not an appropriation, then you are telling us you would not seek additional appropriations for this even though you may have the new additional authorization. Is that correct?

Dr. KINNEY. I think that would have to be a decision that would have to be made after——

Mr. SKELTON. I am asking your present thoughts.

Dr. KINNEY. You are asking for my personal judgment?

Mr. SKELTON. Yes, sir.

Dr. KINNEY. I think no matter what problem we have, no matter whether it is cancer in animals or cancer in humans, additional funds up to a point will contribute to greater advancement in solution of the problems.

But I think one has to very carefully assess the need for those funds and the relative priority, that is, priority relative to other needs.

Mr. SKELTON. My question is this. At the present time, given present circumstances, were you given the authorization that is in the Senate bill before you, would you ask for additional appropriations?

Dr. KINNEY. Mr. Skelton, we have very carefully reviewed the needs for research on animal protection, including the research on bovine leukemia and leukosis and other malignancies. At the present time we have not asked for additional funding.

Mr. SKELTON. The answer would be no; is that correct?

Dr. KINNEY. The answer would be no until we have an opportunity to further assess the probable payoff of such additional funding.

Mr. SKELTON. The last sentence in your conclusive paragraph states this: "Given the basic nature of the research involved, research is being conducted in other Federal agencies directed toward these same underlying factors."

Does that mean animal cancer, the underlying factors?

Dr. KINNEY. What that phrase says is that the research that is being conducted in——

Mr. SKELTON. Just answer my question, sir. What does the phrase "underlying factors" refer to?

Dr. KINNEY. Underlying factors refers to basic research that would have application to cancer research in general.

Mr. SKELTON. You say, then, that other Federal agencies are doing research on animal malignancy. Is that correct?

Dr. KINNEY. They are doing research that is directly or basically related to the solution of some of the problems associated with animal cancer.

Mr. SKELTON. Would you enumerate those Federal agencies with me? Would you tell me what type, in layman's language, of research they are doing, please?

Dr. KINNEY. I think I am going to call on Dr. Splitter after I indicate one obvious one, which would be the National Cancer Institute.

Dr. SPLITTER. I think what Dr. Kinney is trying to emphasize here is the fact—and as Senator Melcher has emphasized—there are interrelationships between the basic causes of cancer——

Mr. SKELTON. Just answer my question. What other Federal agencies are doing animal malignancy research and what type research? That is my question.

Dr. SPLITTER. I think we will have to defer and insert this in the record to have a complete record of the situation.

Mr. SKELTON. I am only asking you for what you have in your statement.

Did you prepare this statement, Dr. Kinney, or was it prepared for you?

Dr. KINNEY. Dr. Splitter, Dr. Purchase and I prepared it.

Mr. SKELTON. Is there anyone on your staff who can answer the question as to what——

Dr. SPLITTER. I might say that the Veteran's Administration has a strong interest in cancer. The FDA has a strong interest in cancer causes. The EPA has a strong interest.

Mr. SKELTON. All of them are doing animal malignancy cancer? That is the question?

Dr. SPLITTER. I would not be able to say to what extent they are doing it.

Mr. SKELTON. I would ask unanimous consent that Dr. Splitter and Dr. Kinney be allowed to answer my question in writing so that we would know what Federal agencies are doing animal malignancy research and the type of animal malignancy research that they are presently doing as you allege in your statement.

Dr. SPLITTER. May I insert that in the record, sir?

Mr. DE LA GARZA. Without objection, any questions that require submission for the record will be accepted.

[The above-requested information follows:]

FEDERAL AGENCIES CONDUCTING CANCER RESEARCH IN ANIMALS

In addition to the Department of Agriculture the following Federal Agencies are conducting animal cancer research:

Department of Commerce
Department of Defense

Department of Energy
Department of Interior
Department of Health and Human Services
Environmental Protection Agency
National Aeronautic and Space Administration
Smithsonian Institution
Veterans Administration

Most of this research centers on the cause, diagnosis prevention and treatment of cancer using animals as experimental models in which results will have implications to the human disease. Some research also is concerned with the causes and prevention of cancer in wildlife and the carcinogenic potential for animals and man of a variety of substances present or released into the environment.

Major areas of investigation include:

1. The role of chemical, physical and biological agents in the etiology of cancer.
2. The mechanisms of action at the cellular, subcellular and molecular levels that result in cancer including mechanisms controlling cellular proliferation and immunity to cancer under exposure to carcinogenic agents.
3. Improved procedures for accurate, early diagnosis of cancer or the potential to acquire cancer under exposure to carcinogens.
4. Chemical, physical and biological methods for prevention or treatment of cancer.

Mr. DE LA GARZA. Mr. Fithian?

Mr. FITHIAN. No questions.

Mr. DE LA GARZA. Dr. Kinney, to follow up on that question of Mr. Skelton, and the need to supply for the record, I guess gives basic credence to the proposed findings of Senator Melcher's legislation, that basic research and diagnosis and prevention of tumors in animals and birds has not been adequately coordinated. If it had been coordinated, you could have it at your fingertips here. Who is doing what?

Dr. KINNEY. Our coordination with the groups that have done research on malignancies in farm animals has been primarily with the National Cancer Institute, with a number of the State universities that are conducting research on cancer, a number of private universities, with industry. Those have been our principal cooperators.

Mr. DE LA GARZA. That leads to the next question.

In your statement on page 2, you say: "SEA has a storng program on cancer in animals and basic research on animal reproduction." Where and with whom? Would you supply for us that information?

Dr. KINNEY. Yes, we can supply that. Basically I am referring to our major laboratories at East Lansing, Mich.; at Ames, Iowa; Beltsville, Md.; Clay Center, Nebr.; Miles City, Mont.; Fort Reno, Okla.

Mr. DE LA GARZA. Would you supply for the record what the type of research is that is going on, with whom, and where?

Dr. KINNEY. With whom and where?

Mr. DE LA GARZA. Yes.

Dr. KINNEY. Within our organization?

Mr. DE LA GARZA. You are coordinating with, let us say, Texas A. & M. University. All right. You are doing that. You have to have a list.

Dr. KINNEY. Yes, we can provide that.

Mr. DE LA GARZA. And the specifics, not necessarily in great detail. Do you have grant funding for these institutions? Or does that refer back to basic research in title XIV?

Dr. KINNEY. We have occasionally grant funding, but most of our research is through a cooperative agreement. We have scientists who are cooperating with State scientists or with scientists in other institutions.

Mr. DE LA GARZA. Do you have contract-type work where you contract out to a laboratory or a university?

Dr. KINNEY. Very little in this area of research, if any.

Mr. DE LA GARZA. Please provide that information to us in writing.

Your next paragraph says: "SEA has ongoing programs on the mechanisms of reproduction involving pituitary and gonadal hormoes."

Could you do likewise for that?

Dr. KINNEY. Yes, we can.

Mr. DE LA GARZA. Without objection, so ordered.

[The above-referred-to material follows:]

ANIMAL CANCER RESEARCH
DEPARTMENT OF AGRICULTURE

Research on cancer of food animals is being conducted at the following locations:

SEA/Agricultural Research In-House

Regional Poultry Research Lab, E. Lansing, MI
National Animal Disease Center, Ames, IA
Eastern Regional Research Center, Wyndmoor, PA
Northern Regional Research Center, Peoria, IL
Southern Regional Research Center, New Orleans, LA
Russell Research Center, Athens, GA
Western Regional Research Center, Albany, CA
National Animal Disease Center, Ames, IA
Poultry Research Laboratory, Georgetown, DE
Southeast Fruit & Tree Nut Lab, Byron, GA
NC State University, Raleigh, NC
Veterinary Toxicology & Entomology Research Lab, College Station TX
University of Nebraska, Lincoln, NE
Coastal Plain Experiment Station, Tifton, GA
National Peanut Research Lab, Dawson, GA

Cooperative Agreements

University of Florida, Gainesville, FL
University of Missouri, Columbia, MO
Texas A&M, College Station, TX

Other cooperators include State Agricultural Experiment Stations, Colleges of Veterinary Medicine and Colleges of 1890 in AL, AK, CA, CT, FL, GA, ID, IL, IA, LA, MD, MA, MN, MO, NE, NV, NH, NJ, NY, TX, UT, WA, WI, WV.

Research is being conducted on those cancers of food animals which cause important economic loss and on agricultural toxins which are known or potential carcinogens. Studies on these problems are as follows:

MYCOTOXINS:

Mycotoxins in feeds and foods is receiving major attention. The carcinogenic effects of these toxins are being examined and their role in interference with animal growth, reproduction and resistance to disease are being assessed. Rapid and accurate tests are being sought to detect these toxins and methods are being developed to prevent their occurrence in feeds and foods.

AVIAN LEUKOSIS COMPLEX:

Principal efforts on this disease complex are centering on Marek's disease and lymphoid leukosis. Basic mechanisms of resistance to malignancy in Marek's disease vaccination is under study and causes of occasional vaccine failures are being assessed. Methods are being studied for detection and elimination of the virus from infected flocks. The role of genetics in resistance to lymphoid leukosis is being studied in a coordinated, regional research approach and methods are being developed to increase resistance to these diseases through breeding procedures.

BOVINE LEUKEMIA:

Improved methods are being sought for detecting carriers of bovine leukemia virus. Mechanisms of resistance to the disease are being studied and the feasibility of preventative immunization is being determined. Epidemiologic studies are being conducted in infected herds to determine sources of infection, routes of transmission and means of control. Effectiveness of eradication procedure are being evaluated.

CANCER EYE OF CATTLE:

Mechanisms of resistance to this form of cancer are being studied and procedures for enhancing resistance are being evaluated to prevent or eliminate this disease from affected animals.

BASIC REPRODUCTION RESEARCH

SEA/AR inhouse research on reproduction in food animals is being conducted at the following locations:

Beltsville Agricultural Research Center, Beltsville, MD
U.S. Meat Animal Research Center, Clay Center, NE
Russell Research Laboratory, Athens, GA
U.S. Range & Livestock Station, Miles City, MT
U.S. Sheep Experiment Station, Dubois, Idaho
Southwestern Livestock & Forage Research Station, El Reno, OK
National Animal Disease Center, Ames, IA

Cooperative agreements are in effect at the following locations:

University of Maryland, College Park, MD
University of Maryland Medical Center, Baltimore, MD
UCLA Medical Center, Los Angeles, CA
Albany Medical College, Albany, NY
University of Wisconsin, Madison, WI
Iowa State University, Ames, IA
University of Minnesota, St. Paul, MN
University of Florida, Gainesville, FL
University of North Carolina, Raleigh, NC

The U.S.D.A., SEA/AR national program of research on reproduction includes research on sperm cell preservation and storage, estrous and ovulation control, causes of infertility and factors that influence reproductive efficiency and cause mortality. Both basic and applied studies are underway with food producing animals.

Research on pituitary and gonodal hormones is primarily aimed at studying the effects of these hormones on the estrous cycle, sperm production, embryo survival, and how these hormones influence the sequence of events required for optimal reproductive performance.

Special areas of basic research are as follows:

*Progesterone Synthesis in Dairy Cattle
*Role of Estrogens in Uterine Contraction
Surface Structure of the Female Reproductive Tract of Cows Examined with Scanning Electron Microscope

Effect of Infected Chemicals on Sperm Transport in the Female
Heat Stress Effects on Semen Quality of Bulls
*Etiology of Postpartum Anestrus in Beef Cows
*Estrus Synchronization and Subsequent Fertility in Beef Cows
*Endocrine Mechanisms Associated with Puberty in Heifers
Reduction in Embryo Mortality in the Cow
*Hormonal Mechanisms Involving the Corpus Luteum in gilts
*Estrus and Ovulation Control in Sows

*Mechanisms of Progesterone and Prostaglandin F Synthesis
Methods for Determining the Fertilizing Capacity of Sperm
Methods for Preservation of Boar Semen
Effect of Trace Minerals on Reproductive Performance in Swine
Physiological Factors Affecting Embryo Survival in Swine
Effect of Nutrition on Sexual Maturity in Swine
Relation of Steroid Hormone Levels in the Blood to Embryonic Development and Survival
*Sperm Transport at Induced Estrus of Anestrus Ewes
*Hormonal Treatment of Rams to Improve Semen Quality
*Role of Estradiol in Ram Fertility
*Effects of Gonadotropin and/or Prostaglanlin on Reproduction of Sheep
Diagnosis of Pregnancy in the Ewe
Preservation of Semen for Artificial Insemination in Chickens
*Hormone Mechanisms in Ovulation in the Hen
*Role of Hormones in Controling Broodiness in Hens
*Studies on Pituitary Prolactin in Turkeys

* Areas of research related to pituitary and gonadol hormones

AREAS OF BASIC RESEARCH IN ANIMAL REPRODUCTION AT LAND GRANT INSTITUTIONS AND TUSKEGEE INSTITUTE

(*Areas related to pituitary and gonadal hormones)

TUSKEGEE INSTITUTE

Water quality and artificial insemination
Seminal antigens and sterility
Behavioral causes of abortion

AUBURN UNIVERSITY

Reproductive performance of artificially inseminated broiler breeders
Selected reproductive phenomena in swine and cattle
Neurology of the reproductive system in bulls

UNIVERSITY OF ARKANSAS

Preservation of chicken and turkey sperm
Secretions of the oviduct and uterus in ewes
*Function of gonadotropic hormones on corpora lutea maintenance and secretions
Metabolism of the fetal and neonatal ruminant
*Hormones and external phenomena affecting gonad and accessory gland function

UNIVERSITY OF CALIFORNIA

*Endocrine control of the estrus cycle in mares
Indices of libido
*Female reproductive physiology
Multiple births and embryo transfer in beef cattle
Morphogenesis in avian species
Reproductive efficiency of turkeys and freezing of semen
Biochemistry of fertilization and hatching
Biochemistry of embryo development in mammals

COLORADO STATE UNIVERSITY

*Sheep uterine estrogen receptors
Reproductive efficiency in turkeys

THE UNIVERSITY OF CONNECTICUT

Embryo mortality and hatchability

UNIVERSITY OF FLORIDA

*Luteolytic process in mares
*Onset of estrus and ovulation in mares
*Multiple births and ovulation control
Uterine secretions and embryoric survival

UNIVERSITY OF GEORGIA

Avian sperm-survival and contribution to embryo viability
*Endocrine and physiological aspects of embryo survival in swine
*Endocrinolgy of reproduction in beef and dairy cattle
*Endocrine control of testosterone secretion

UNIVERSITY OF ILLINOIS

*Re-establishing ovarian cycles in the postpartum cow
*Factors affecting parturition
Nutritional factors influencing reproduction
*Endocrine factors influencing reproductive performance of dairy cattle
Reproductive performance and cytogenetics of newborn calves
*Hormonal control of the testes
Embryo genesis
Mammalian acrosomal enzymes

PURDUE UNIVERSITY

*Pituitary hormones and reproduction
Sperm maturation, capacitation and fertilization
Biochemical and metabolic disorders associated with parturition

IOWA STATE UNIVERSITY

*Improving postpartum fertilization

KANSAS STATE UNIVERSITY

Embryonic development in swine

UNIVERSITY OF KENTUCKY

*Lactation, prostoglandins and reproductive efficiency in sows
*Ovarian response to infusion of glucose and amino acids in ewes
*Postpartum reproduction in mares
*Effect of the blastocyst on maternal recognition of pregnancy in the mare
*Factors related to non-cycling in dairy cattle
*Reproductive pauses in poultry

LOUISIANA STATE UNIVERSITY

*Physiology of reproduction-cattle, swine and horses
Fetal effects on fetal size
Bovine sperm morphology and physiology

SOUTHERN UNIVERSITY

*Control of estrus in dairy cattle
Adrenal effects on reproduction in poultry

UNIVERSITY OF MASSACHUSETTS

Chromosome mapping

UNIVERSITY OF MARYLAND

*Controlled ovulation and pregnancy

MICHIGAN STATE UNIVERSITY

*Hormonal control of ovulation in cattle and sheep
*Neuroendocrinology of lactation, reproduction, tumors and aging
*Hypothalamic-hypopheseal-gonadal relationships in cattle
*Ovulation in mares
Improvement of fertility and reduced embryonic loss in swine
Reproductive efficiency in turkeys
*Regulation of follicle growth

UNIVERSITY OF MINNESOTA

Preservation of germ cells, tissues and organs
*Physiology and chemistry of the male genital tract
*Endocrine and neurological regulation of reproduction in poultry
*Seasonal infertility in swine

UNIVERSITY OF MISSOURI

*Biochemical aspects of reproduction in farm animals
*Endocrinology of bovine reproduction
*Postpartum fertility in dairy cattle
*Effect of confinement on reproduction in swine

LINCOLN UNIVERSITY

*Corpora lutea function in domestic animals
The fate of sperm in cattle and sheep
Life span of the corpora lutea in estrus synchronization in sheep

NORTH CAROLINA STATE UNIVERSITY

Estrus cycle and uterine substrate utilization
*Nutrition related to hypothalamic, hypophyseal and testicular function in bulls
*Control of follicle stimulating hormone in cattle
*Neuro-endocrine-gonadal development and semen production
*Endocrinology of postpartum anestrus and pregnancy maintenance
Role of selenium and vitamin E in the fertilization of sheep ova

UNIVERSITY OF NEBRASKA

Physiological aspects of bovine reproduction
Cytogenetics and fertility in dairy cattle
Physiology and genetics of ovulation rate in swine
*Endocrinology of puberty and estrus in gilts

UNIVERSITY OF NEVADA

Ova transplantation in cattle

UNIVERSITY OF NEW HAMPSHIRE

Control of ovulation in dairy cattle

RUTGERS UNIVERSITY

Ovarian function in laying hens

NEW MEXICO STATE UNIVERSITY

*Progesterone, pituitary hormones and reproduction in ewes

CORNELL UNIVERSITY

Sperm production, freezing and fertilization
*Placental lactogen and estrus
Ovulation in chickens
Development of avian embryonic integument
Nutrition and development of the chick embryo

OHIO STATE UNIVERSITY

*Endocrinology of male infertility
Turkey semen and artificial insemination
Chromosome aberrations
Role of the uterus in litter size in swine

OKLAHOMA STATE UNIVERSITY

Role of the sperm acrosome
*Endocrine relationships to embryogenesis and heat stress in swine
*Postpartum anestrus in beef cattle

OREGON STATE UNIVERSITY

Factors affecting reproductive capacity of farm animals

PENNSYLVANIA STATE UNIVERSITY

*Controlled ovulation in dairy cattle
Immunological aspects of the maternal-fetal relationship
*Gonadotropin secretions and testicular function
Functional aspects of spermatozoa

UNIVERSITY OF RHODE ISLAND

Controlled ovulation and pregnancy
Artificial insemination and fertilization in caged layers

CLEMSON UNIVERSITY

In-vitro culture of chick embryos
*Pituitary function and postpartum estrus in beef cattle
Role of the uterus in embryo survival in dairy cattle
Exogenous hormonal control of reproduction
Semen preservation-chickens and turkeys

SOUTH DAKOTA STATE UNIVERSITY

Placental transfer of iron

UNIVERSITY OF TENNESSEE

*Transfer of endocrine molecules across the uterine barrier

TEXAS A&M UNIVERSITY

Embryo transfer
Reproductive physiology of turkeys
Response of bovine embryos to endogenous chemicals
*Breed effects on the endocrinology of cattle

VIRGINIA POLYTECHNIC INSTITUTE AND STATE UNIVERSITY

Sperm-oviduct interrelationships in fowl
Germ cell structure and function
Specific enzymes of bovine sperm
Porcine placental function

UNIVERSITY OF VERMONT

*Controlled ovulation in cattle

UNIVERSITY OF WISCONSIN

*Control of corpora luteal function
Post-partum infertility in cattle
*Luteal function and embryo survival
Sperm maturation and preservation

WASHINGTON STATE UNIVERSITY

*Hypothalamic hormones and reproduction
Critical processes in artificial insemination

WEST VIRGINIA STATE UNIVERSITY

Controlled ovulation and pregnancy

UNIVERSITY OF WYOMING

*Endocrinology of postpartum period

Mr. DE LA GARZA. In that, we want what programs, whom you
e working with, their names and locations.
You also state, for example, the vaccine that has been developed
r poultry. Would you give us a little bit more on that, who did
ie basic research and how it evolved and your participation? Just
ve us a little brief history of that, if you would. Can you do that
ow?
Dr. KINNEY. I think I can give you a brief history on that
ecause it is a good example. It points out the complexity of doing
esearch on something like animal cancer or leukosis in this specif-
case, Marek's disease.
This research really started in 1939. It went on for over 20 years
efore it was even realized that we were working with a complex of
iseases, lymphoid leukosis, and Marek's disease.
It was only at that point, after we were able to define the
rganism, or the fact that there were two diseases that we went on
or another decade doing research on a specific disease, Marek's
isease, before we rather serendipitously discovered that it was a
irus. From there it was all downhill, once we discovered what the
irus was and so forth.
We worked on it for over 30 years before there was even an idea
f a breakthrough in developing a vaccine. So, much of the work
hat is done is discovery work. It is very basic research. Some of it
s slippage, absolutely worthless research. But it is research that
ne has to go through in order to eliminate causes.
We can supply a more detailed breakdown for the record.
Mr. DE LA GARZA. If you would, for the record.
Without objection, so ordered.
[The above-referred-to material follows:]

DEVELOPMENT OF THE MAREK'S DISEASE VACCINE

Mortality among laying chickens became a very pressing problem in commercial flocks throughout the United States between 1925 and 1937. This was a period when there was very rapid growth in the commercial poultry industry. A large portion of the mortality was attributed to one or more cancerous diseases included in what was later referred to as the avian leukosis complex. Research to determine the causes of the avian leukosis complex, to identify the separate disease entity of Marek's disease and to develop its preventative vaccine spand a period from the 1930's to the 1970's. Research participants in this successful effort included U.S.D.A. SEA/Agricultural Research (SEA/AR) and cooperators in the State Agricultural Experiment Stations and Colleges of Veterinary Medicine in AL, AR, CT, DE, GA, IA, ME, MD, MA, MI, MN, MO, NH, NJ, NY, OH, PA, RI, WA, WV, WI and England's Houghton Poultry Research Station.

Intensive work on the avian leukosis complex was initiated by the U.S.D.A. following the establishment of the Regional Poultry Research Laboratory in 1939. At this point in time "leukosis" of chickens was considered to be a neoplastic disease of unknown etiology. Research progress by SEA/AR and its cooperators in the 1940's and 1950's led to the theory that the avian leukosis complex was caused by a single group of leukosis viruses causing neural, visceral and ocular lymphomatosis. In the 1960's it became apparent that two groups of viruses were involved and more recently a third agent, known as reticuloendotheliosis virus, has been found to be another cause of avian leukosis.

Marek's disease had been confused with lymphoid leukosis because of the similarity of lesions of the two diseases. In the 1950's Marek's disease, although not given the name at that time, seemed to increase in incidence in the United States. A similar form of the disease appeared in Great Britain in 1965 and intensive studies also were initiated there at Englands' Houghton Poultry Research Station.

In 1967 scientists at the Regional Poultry Research Lab and at the Houghton, England laboratory concurrently and independently found that the avian leukosis complex is in fact at least two separate diseases - lymphoid leukosis and Marek's disease - each caused by different viruses. In 1969 multiplication of Marek's disease virus was found to be centered in feather follicles by SEA/AR and New York scientists. A related virus was discovered in turkeys by SEA/AR and Wisconsin scientists. Attenuation of Marek's disease virus was found to protect against the disease by Houghton, England scientists. SEA/AR scientists demonstrated that the turkey virus protected chickens against Marek's disease under laboratory conditions. In 1970 SEA/AR scientists and subsequently State cooperators and others showed the value of the turkey virus as a vaccine for preventing Marek's disease under field conditions. The vaccine was licensed by Michigan for use in that state in 1970. In 1971 the vaccine was licensed for nationwide use by the U.S.D.A.

Mr. DE LA GARZA. You state that this was a well-coordinated effort by SEA and its cooperators. We would like to know a brief history, who the cooperators were in that material. I am not the most versed on this, but to my knowledge that would be the only vaccine that exists for cancer either for man or animal.

Dr. KINNEY. To my knowledge it is the only known vaccine for a cancer.

Dr. SPLITTER. This is the first commercially available and successful vaccine for cancer, man or animal.

Mr. DE LA GARZA. What one questions at this time is that it seems to be such a sensational breakthrough. You do not hear from the human side.

To what extent has there been joint work? To what extent, to your knowledge, is this vaccine or the research on it, has there been an attempt to translate that to the possibility of a vaccine in human cancer?

Dr. SPLITTER. Of course, we have different disease cancer problems in people. In Marek's disease, the most closely related possibility is human leukemia. As yet we have no vaccine in bovine leukemia, but we have the virus isolated. So, we cannot translate directly to the human and say that a poultry vaccine should also result in a human vaccine because the diseases are entirely different.

Mr. DE LA GARZA. I understand that. But the basic theory is if they found a vaccine that will attack a carcinogen or a tumor or cancer in poultry, all you hear on the human side is that they are still looking.

I know there are different kinds of cancers caused by different carcinogens or viruses, or whatever affects the system. I know that, but what I would like to know from you is to what extent have the developers of this vaccine, at whatever level it is that you have coordination, brought the working papers?

Dr. SPLITTER. There have been joint discussions in the area of leukemia for a good number of years between the National Institutes of Health and the Department of Agriculture and others. The scientists there are well aware of this discovery.

Mr. DE LA GARZA. Do you go to them or do they come to you?

Dr. SPLITTER. It works both ways, sir.

Mr. DE LA GARZA. You cannot tell at one time who came to whom?

Dr. SPLITTER. There are international meetings which are planned involving the whole community interested in leukemia. There are other meetings locally.

Mr. DE LA GARZA. That was my next question. To what extent is all of this research involving the international community? Do you coordinate with other countries? If other countries are doing basic research also, to what extent do you coordinate?

I do not mean international meetings where you have a symposium in London or in Las Vegas or something like that. I mean actual day-to-day coordination.

Dr. SPLITTER. We have international exchange programs with a variety of countries where they exchange scientific information. We have visiting scientists from many countries coming here and our scientists going to those countries. There are a wide variety of

these types of programs sponsored by the Department and by the Agency for International Development.

Dr. KINNEY. So far as international cooperation is concerned, in my opinion, it is excellent. The research team at East Lansing, I believe 4 of the 12 members of that research program, have, in the last several years, spent at least a year working in a counterpart laboratory in Germany, England, Austria, or other countries.

We do regularly allow these people to spend a sabbatical-type leave in other laboratories overseas or in this country doing the same sort of research.

Mr. DE LA GARZA. Are there any further questions of Dr. Kinney?

Mr. WAMPLER. Dr. Kinney, I appreciate your candid way of responding to questions.

I guess I find myself somewhat frustrated year-in and year-out regardless of which administration is in power. It seems that the Department of Agriculture does not get the request for what I perceive of as adequate funding to carry out these basic essentials of research.

Under the new budgetary process that we have here in the House and the Congress, this committee has the responsibility to make recommendations to the House Budget Committee in those categories affecting agriculture as to what we think an adequate funding level should be or realistically what we can expect by way of appropriations.

What happens so frequently is that people in the Department, as this information has been made available to this committee, do not ask for this money.

What I am saying is if you do not ask for it, you do not get it. I am just as much in sympathy and support for the concept of a balanced budget as the next person. But what has happened through the years is that our research efforts in the Department of Agriculture, where we are talking about diseases of animals, those affecting cancer research and other types of research, have been diminished.

Our effort has not been increased as Congress mandated be done in title XIV of the 1977 farm bill. There are many important areas of research that have not been funded with $1. Part of that is the fault of the Congress.

But unless those of you who are administering those programs ask for that funding, you certainly are not going to get it, particularly in light of today's fiscal situation. I want to encourage you and others to look at these programs realistically. I can give you a good example.

Our land-grant university in Virginia does a great deal of research on diseases of animals. Some is supported through the traditional form of funding that goes to our land-grant colleges. Some has been financed through State funds. A great deal of it has been financed from the private sector, from segments of agriculture that have a particular interest.

I recall that a scientist in the Department of Animal Sciences made a spectacular breakthrough in developing a vaccine affecting diseases of the herpes. This was done basically with private and State funds.

I think you well pointed out that in basic research sometimes you do not make a spectacular finding, but you eliminate possible causes or areas. This again is in the total concept of research.

Too, I think some of the most significant breakthroughs that have occurred have been somewhat accidental or as a corollary of basic research going on. An example is the discovery of the Salk vaccine.

I suspect someday someone is going to develop a vaccine that will immunize us against cancer or certain types of cancer. This is why we feel so strongly that this basic research on cancer in cattle and poultry and birds indeed is of the highest priority. This is why we would like to see it move forward. We think it is terribly important.

I want to encourage you to look realistically. I recognize there are those above you who tell you what level of funding you can have. But unless you ask for it and make your case, I do not think you are ever going to get the funding we feel you should have and which I think you need.

I make that observation to you. I hope you will look at this realistically. In my judgment, the need is there. We hope that we can give you money that you can spend wisely. My guess would be that you have a large number of applications for grant research that you cannot fund because you do not have the money to do so. And I think it would be meaningful research.

I recognize the role that you are here today in, but in the future I hope you ask for money that you think is needed. Then let those above you make a judgment.

Thank you.

Dr. KINNEY. Thank you, Mr. Wampler. You are very perceptive.

Mr. DE LA GARZA. Thank you, Dr. Kinney. I guess your organization suffers from the same problem that this committee suffers from. There are lines on the other side of the Capitol waiting to get into a hearing room to find out if Billy Carter got money from the Libyans or did not get money from the Libyans.

Here I think we have about 30 people. Yet, you tell us that part of your work has reduced from $200 million to $30 million losses to the agricultural sector of the United States. It went from $200 million to $30 million.

I would suggest it would merit headlines in every paper in the United States, but the headlines are saying whether Billy went to Libya or not. So, I guess that is something that you and we have to suffer from, being in the nonsensational part of our Government.

We commend you for the excellent work you have done. I would like to echo the words of my colleague, the distinguished gentleman from Virginia, Mr. Wampler. It is not whistle-blowing. It is not being disloyal. It is not anything but commonsense.

You, at whatever level you can, communicate your basic needs. This is entirely proper and responsible so that we may know the basic facts. Then we will know where or who or what is causing the problem.

If we are going to assist you, we need to have the basic facts in the beginning. Then we will try to assist as we have done. Title XIV of the 1977 act was done, the major work, by Mr. Wampler with basic research from the people out in the field and from the

different agencies in a responsible manner and somewhat against the grind as related to the Secretary of Agriculture and the administration at that time. It is a proper and responsible way to coordinate and communicate with us.

Dr. KINNEY. I am very appreciative of the action that was taken in title XIV. Quite particularly I appreciate the attention and support that has been given for basic research very recently. It is very badly needed because it does represent our total future in agriculture.

Mr. DE LA GARZA. Thank you very much, sir. We appreciate your cooperation and that of your colleagues.

Our next witness is Dr. Dale K. Sorensen of the University of Minnesota for American Veterinary Medical Association and the Association of American Veterinary Medical Colleges.

Dr. Sorensen, we welcome you. We would be very happy to hear from you at this time.

I might add at this time for the rest of the witnesses that without objection your full statements will appear in the record if you care to summarize or shorten in any way.

Also, we will go through the next three witnesses and not yield for questions at the end, but rather have all three available.

Is Dr. Naughton here?

Dr. NAUGHTON. Yes.

Mr. DE LA GARZA. If we can have you this morning and not have you come back this afternoon, we will try to do so.

STATEMENT OF DR. DALE K. SORENSEN, COLLEGE OF VETERINARY MEDICINE, UNIVERSITY OF MINNESOTA, REPRESENTING AMERICAN VETERINARY MEDICAL ASSOCIATION AND ASSOCIATION OF AMERICAN VETERINARY MEDICAL COLLEGES

Dr. SORENSEN. Thank you, Mr. Chairman.

Mr. Chairman and members of the subcommittee, the American Veterinary Medical Association and the Association of American Veterinary Medical Colleges appreciate this opportunity to appear before the subcommittee in support of S. 2043.

I am a member of the American Veterinary Medical Association's Council on Research, and I am Associate dean for academic affairs and research, College of Veterinary Medicine, at the University of Minnesota.

I speak for the American Veterinary Medical Association, which represents about 32,000 member veterinarians, and the Association of American Veterinary Medical Colleges, which represents the 25 colleges of veterinary medicine and the departments of veterinary sciences of the colleges of agriculture of the United States.

It is a pleasure for me to present a brief summary of cancer in animals and the impact that this problem has in the United States.

Cancer is a disease not unique to man. It knows no species barriers, affecting all species of domestic animals, wildlife, and poultry. Various types of tumors have been encountered in many vertebrate species, including mammals, birds, and reptiles. Fish are also susceptible to this disease. There is a greater concern of cancer in the domestic species of animals than in the nondomesticated since it has a greater impact on man and our quality of life. Cancer

in animals and poultry affects the food supply of the Nation as affected animals or birds cannot be utilized for human consumption. Malignant tumors in companion animals or pets cause disruption to family life as well as cost consumers considerable expense for veterinary medical care to manage the ill patient. The potential public health hazard of animal neoplasia is of concern and needs greater definition.

There is an urgent need to increase the emphasis of cancer research on domestic animals and poultry. The primary basis for this need is to develop better methods for the diagnosis, control, and prevention of cancer in food-producing animals and poultry. There is also a need for improved diagnostic and therapeutic methods for cancer of companion animals. Companion animals play an extremely important role in maintaining the mental health of millions of Americans. Pets are essential members of families and necessary for happiness and a high quality of life for many people. It is also well-recognized that animals provide excellent models for biomedical research on oncology. Increased knowledge of animal oncology will lead to a greater utilization of animals in solving human cancer problems.

A better understanding of the needs for additional funds to conduct research on neoplasia may be gained by reviewing some data. I would like to first turn to the prevalence of neoplasms in food, animals and poultry.

Reliable data is available on the prevalence of neoplasms in food-producing animals and poultry from the Federal meat and poultry inspection program, Food Safety and Quality Service, U.S. Department of Agriculture.

Animals and birds sent to slaughter are subjected to ante mortem and post mortem inspection to insure wholesomeness for human consumption.

There are several tables that I would like to have inserted in the record which provide data on the prevalence of animal neoplasms for 1978.

Mr. DE LA GARZA. Without objection, so ordered.

Dr. SORENSEN. I would like to add that updated tables have been provided and prepared for the calendar year 1979.

The updated information for 1979 depicts essentially the same data. It illustrates that the actual level of animal neoplasia remains rather constant.

I might make one additional note and that is that in the case of birds for 1979, the total number of birds that were condemned increased to about 4.6 million over 3.9 million in 1978, indicating that there is still a good deal of neoplasia in birds remaining in this country.

The rest of the data is very comparable between the 2 years.

[The tables appear at the end of the statement.]

The data presented in these three tables provides some useful information on the importance of neoplastic diseases in food-producing animals and poultry in the United States. It should also be kept in mind that this represents only the animals and birds that were processed through federally inspected plants in the United States. The percent of animals and birds slaughtered in federally inspected plants varies with each animal species and ranges from

approximately 86 percent to 96 percent. These are perhaps very liberal assessments on this particular point.

I would now like to turn to the estimated economic loss due to neoplasms in food animals and poultry.

The economic loss due to cancer in food animals and poultry can be estimated utilizing meat and poultry inspection service data on the number of animal carcasses or parts of carcasses condemned for neoplasms. It is also necessary to include the economic loss associated with veterinary medical services for a portion of these animals. For example, many livestock producers will have utilized veterinary medical services to diagnose the animal's disease problem. In the case of the squamous cell carcinoma of the eye, the most prevalent neoplastic disease of cattle, surgical treatment is frequently employed. There is also an indirect loss associated with premature or unscheduled loss of animals from the breeding herd as it may reduce potential producvitity of the herd.

It is very, very difficult to get an assessment on this economic loss.

There appears in my testimony a table on the estimated economic loss in 1978. I would ask that it be included in the record.

Mr. DE LA GARZA. Without objection, so ordered.

[The table follows:]

Estimated economic loss in 1978

Loss due to condemnation of animal carcasses or parts	$17,500,000
Loss due to condemnation of poultry and cost of vaccination and control program	30,000,000
Loss associated with decreased productivity	2,000,000
Loss associated with veterinary medical care	2,006,000
Total	51,500,000

Dr. SORENSEN. As Dr. Kinney just testified, our annual loss for Marek's disease is approximately $30 million alone. So, the total economic loss in 1978 is in excess of $51 million.

This figure represents a conservative assessment of the annual economic loss associated with cancer of food-producing animals and poultry. It is recognized that the carcasses condemned are utilized for other nonhuman products, but all carcasses condemned represent a direct total loss to the producer and, ultimately, to the consumer in higher prices for the product.

In food-producing animals and poultry there are three economically important neoplastic diseases. In cattle the two important diseases are bovine leukeosis, or leukemia, and squamous cell carcinoma of the eye.

I should add here that in the tables squamous cell carcinoma of the eye is really referred to as epithelioma, as this is the terminology used by the Meat Inspection Service.

The prevalence of squamous cell carcinoma in adult Hereford cattle may be as high as 20 percent to 30 percent and it represents the leading cause of condemnations at slaughter.

In the case of bovine leukosis or leukemia, seriologic studies suggest that approximately 10 percent of adult dairy cattle are infected with leukemia virus necessary for the disease to develop. Meat inspection data shows that this is the second leading neoplastic disease.

Another cause of economic loss is associated with the export of purebred cattle. In 1978 the United States exported 122,000 breeding cattle with a value of $94 million.

Some potential importing countries, for example Yugoslavia, prohibit the import of U.S. cattle due to the presence of bovine leukemia virus infection in dairy herds. In the future, we may be unable to export breeding cattle to foreign countries with control programs for leukosis unless we have a similar level of control.

Both of these diseases are very prevalent diseases by any standard used for comparison. In the case of poultry, the most common neoplastic disease is Marek's disease. Prior to the development and use of a vaccine, Marek's disease constituted an extremely serious economic threat to the poultry industry.

Losses were estimated to be in excess of $150 million annually in the United States. Losses still occur because the vaccines are not 100 percent effective and there is concern about the emergency of more pathogenic strains of the virus.

I turn now to neoplasms in companion animals.

Companion animals such as dogs and cats frequently develop cancer. In fact, the prevalence is greater in companion animals than in food-producing animals because the lifespan of farm animals is shorter than for pets and there is less time for diseases of old age, such as neoplasms to be expressed.

The occurrence of tumors in dogs and cats hospitalized in veterinary teaching hospitals in 12 veterinary colleges in the United States was reported for a 5-year period--1964 to 1969. This study revealed a 5.5 percent increase of tumors in over 100,000 hospitalized canine patients. Malignancy is one of the most important causes of deaths in dogs.

There is an urgent need for research to develop improved methods in cancer diagnosis and therapy. Veterinary oncology is just developing and needs research findings to improve the quality of care for patients and for the control of these diseases.

One cannot assess an economic value on the problem of cancer in companion animals or the cost of providing veterinary medical care for these animals, but it certainly involves several millions of dollars annually.

I turn now to cancer in zoo animals, wildlife, and fish.

Neoplasia has been reported in virtually all animal phyla. The incidence rates of tumors encountered in this broad range of species has not been studied. There is little information available except for reports of various tumors in the many species of mammals, birds, reptiles, and fish. Funds are needed for research to provide more information on the extent of neoplasms in this group and to develop approaches for cancer therapy in zoo animals.

I turn now to human health hazards of animal cancer.

There is no evidence as yet that the bovine leukemia virus possess any danger to man. This virus infects sheep and goats and it is oncogenic in sheep.

Investigators have not found antibodies to bovine leukemia virus in the sera of cancer patients or of normal humans from high risk groups. At the present, bovine leukemia virus is an adulterant in our meat and milk which could be prevented if additional technology was known. The virus can be propagated in mammalian cells

and nonhuman primates. This has caused concern in the scientific community. There has been similar concern with Marek's disease. There is no evidence linking this disease with human infection or cancer, but further studies are warranted.

I turn, in summary, to the role of animal cancer for biomedical research.

We believe that there is a need for providing funds for research on cancer problems in domestic animals, poultry, and wildlife. We believe that an urgent need exists from both economic and humanitarian viewpoints. We believe that it will be a good investment and that future cost-benefit analysis will be able to demonstrate it in the area of food-producing animals and poultry.

We are in total support of this bill to provide for research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife. It will provide emphasis on animal cancer problems and a basis for financial support of essential research.

I have a few additional comments that I would like to make that are not in my prepared statement.

There is a great concern among the veterinary colleges about the lack of research funds to conduct research on cancer problems in animals. Currently in general, there are only two major potential Federal sources of support funds.

The National Cancer Institute provides support for projects on animal cancer, demonstrating either a potential human health hazard or an animal model of a similar type cancer in man.

This severely limits the type of oncogenic research which is eligible for NCI funding.

The other source is the Science and Education Administration of the U.S. Department of Agriculture. They have supported research on economically important neoplastic diseases of animals and poultry in the past and indicate continued support for economically important cancer programs.

But funding levels for animal health research and disease priorities restrict and limit the cancer disease problems that are eligible for funding from SEA.

In assessing the situation, there is no Federal granting agency that is supporting research on cancer in animals or birds with emphasis on protecting the health of domestic animals, poultry, and wildlife.

It is believed that basic research in animal cancer will ultimately lead to a better understanding of all types of cancer. The potential benefit of this type of research to assist in solving the human cancer problem would be greatly increased.

I would like to close with just an assessment that developed out of previous discussions.

In the area of biomedical research, animal models appear to be the only rational means by which the effect of immunological manipulations can be assessed. To utilize in human immunotherapy any empirical technique that has not yet been demonstrated to be effective in animal models is dangerous.

There is a good deal of hope in the scientific community that immunological manipulations can induce a degree of truly effective immunity which will permit the destruction of tumors or the few

or cells that may remain after surgery, radiotherapy, or chemo-
apy.
elieve there is just an urgent need for additional research in
rea of animals for biomedical research.
e thank you for this opportunity to express our views.
r. DE LA GARZA. Thank you. We invite you to remain for
tions after the other witnesses.
e have a vote now. We will recess and be back shortly.
ecess taken.]
he tables referred to previously follow:]

Table 1. NUMBER OF ANIMAL CARCASSES CONDEMNED FOR NEOPLASIA IN 1978

Neoplasm	SPECIES Cattle	Calves	Sheep	Swine	Horses
Carcinoma	3,303	7	31	444	36
Epithelioma	16,833	38	3	104	3
Leukosis (Leukemia)	7,945	128	42	1,316	15
Sarcoma	325	10	8	835	119
Misc.	316	16	7	632	41
Totals	29,222	199	91	3,331	214

Table 2. NUMBER OF ANIMAL CARCASSES CONDEMNED FOR NEOPLASIA IN 1979

Neoplasm	SPECIES Cattle	Calves	Sheep	Swine	Horses
Carcinoma	3,035	19	32	921	134
Epithelioma	15,721	8	-	-	5
Leukosis (Leukemia)	7,461	60	28	1,258	46
Sarcoma	244	6	8	369	31
Misc.	555	9	7	669	43
Totals	27,016	102	75	3,217	259

Table 3. NUMBER OF ANIMAL CARCASSES WITH PARTS REMOVED DUE TO NEOPLASIA IN 1978

Neoplasm	SPECIES Cattle	Calves	Sheep	Swine	Horses
Epithelioma	75,267	328	190	295	3
Misc.	2,059	23	5	994	64
Totals	77,326	351	195	1,289	67

Table 4. NUMBER OF ANIMAL CARCASSES WITH PARTS REMOVED DUE TO NEOPLASIA IN 1979

Neoplasm	SPECIES Cattle	Calves	Sheep	Swine	Horses
Epithelioma	69,715	102	-	-	1
Misc.	1,950	12	3	1,492	78
Totals	71,665	114	3	1,492	79

Table 5. NUMBER OF BIRDS AND PERCENT CONDEMNED FOR NEOPLASIA DURING CALENDAR YEAR 1978

Class of Poultry	LEUKOSIS Number	Percent to Total
Young Chickens	3,633,324	.10
Mature Chickens	308,375	.16
Fryer/Roaster Turkeys	253	*
Young Turkeys	2,425	*
Old Turkeys	112	.01
Ducks	286	*
Other Poultry	11	*
Totals	3,944,786	

Table 6. NUMBER OF BIRDS AND PERCENT CONDEMNED FOR NEOPLASIA DURING CALENDAR YEAR 1979

Class of Poultry	LEUKOSIS Number	Percent of Total
Young Chickens	4,309,496	.11
Mature Chickens	275,770	.14
Fryer/Roaster Turkeys	762	.01
Young Turkeys	3,160	*
Old Turkeys	101	.01
Ducks	94	*
Other Poultry	50	*
Totals	4,589,433	.11

*Less than one-hundredth of 1 percent

Fourth leading cause of poultry condemnations

Mr. DE LA GARZA. The subcommittee will be in order.

The next witness is Dr. Robert R. Marshak, dean, Veterinary School of Medicine, University of Pennsylvania. I understand he will be accompanied by Dr. Jorge Ferrer, professor of clinical studies, New Bolton Center, University of Pennsylvania.

We welcome you and will be happy to hear from you at this time.

STATEMENT OF DR. ROBERT R. MARSHAK, DEAN, VETERINARY SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA, ACCOMPANIED BY DR. JORGE F. FERRER, PROFESSOR OF CLINICAL STUDIES, NEW BOLTON CENTER, UNIVERSITY OF PENNSYLVANIA

Dr. MARSHAK. Thank you, Mr. Chairman. I am deeply grateful for this opportunity to speak in support of S. 2043, the Animal Cancer Research Act. My name is Robert Marshak.

My colleague is Dr. Jorge Ferrer, a professor of microbiology and chief of our section of oncology in our school of veterinary medicine. He is a physician and a tumor immunologist.

So that you will know the biases I may express in this testimony I should tell you that I was a practicing veterinarian in Vermont where most of the people I served for 11 years were farmers with small dairy herds. At that time I was also engaged in clinical research. In 1956 I became a professor of medicine at the School of Veterinary Medicine of the University of Pennsylvania.

Mr. Chairman, my school is part of a great academic health center, including a medical school, children's hospital, a dental school, a major general hospital, and several special research institutes, all working in close association with the Wharton School of Business & Finance, as well as the engineering and other faculties on which the school of veterinary medicine can rely for collaborative research and consultation. Our school is a regional resource. We have contracts to provide veterinary medical education with Puerto Rico and with the States of Maryland, Delaware, New Jersey, Maine, Vermont, Massachusetts, Rhode Island, New Hampshire, and Connecticut.

I have been dean of the Pennsylvania Veterinary School for over 6 years.

Our medical complex has a long history of contributions to cancer research. I began my own research 21 years ago on bovine leukemia and ultimately founded the university's comparative leukemia studies unit at new Bolton Center, the veterinary school's thousand-acre rural campus.

During the past 10 years, under the leadership of my successor, Prof. J. F. Ferrer, a physician/tumor-immunologist who is with me today, the leukemia studies unit has grown into the largest bovine leukemia research program in the western hemisphere. A great deal of what is known about bovine leukemia was worked out in Dr. Ferrer's laboratory.

Over the years since 1959 many agencies have approved our research and supplied it with funds, such as the National Cancer Institute, the American Cancer Society, the World Health Organization, the U.S. Department of Agriculture, the Pennsylvania Department of Agriculture, and the Wetterberg Foundation.

1964, with a grant from the National Cancer Institute, we chased a large commercial purebred Jersey cattle herd with an raordinary incidence of leukemia—78 confirmed cases in a popu- on at risk of less than 400 animals. This herd can only be cribed as a unique national cancer research resource. The NCI ifies these large expenditures on the basis of the value of the ine leukemia system as a model for studies of leukemia in nans.

nfortunately, despite the extraordinary present and potential nomic importance of bovine leukemia and of bovine leukemia is infection to livestock agriculture and to the dairy industry, USDA dollar contribution to our research has been relatively gnificant, never greater than $30,000 per year and today noth- at all.

his distressing reality is the principal reason for my vigorous port of the Animal Cancer Act. It is my fervent hope that ctment of S. 2043 will lead to the appropriation of sufficient lars to erable the USDA to fund extramural research on bovine kemia and other animal cancers at a level consonant with the ntific opportunities we know about, but which are not now ng exploited, and at a level consonant with the economic losses taxpayer and the livestock and dairy industries are now suffer- . Indeed, it is no exaggeration to state that the bovine leukemia blem alone is more than sufficient reason to enact S. 2043.

Consider the following points:

One, bovine leukemia is the most damaging and widespread ncer of dairy cattle. Approximately 30 percent of the dairy cattle the United States are infected with bovine leukemia virus. vine leukemia virus is also widespread in the beef cattle popula- n.

Two, whereas only certain cattle with a given genetic constitu- n develop tumors when infected, bovine leukemia virus is shed milk and perhaps also in other secretions and excretions of fected animals. Bovine leukemia virus, which we call BLV, is ghly contagious, spreading from infected to noninfected cattle by ntact.

Three, with the possible exception of bluetongue, bovine leuke- a virus infection is the greatest single threat to the large Ameri- n cattle export business. Most countries of the world do not allow e importation of bovine leukemia virus infected cattle or of men from infected bulls. Indeed, some countries even forbid im- rtation of cattle testing negative for BLV, but which originate om herds where any level of infection is present. We can expect at this wise regulatory policy will one day be applied universally. West Germany, a country with an official BLV eradication pro- am is already displacing the United States in the cattle export siness. This Congress has heard again and again that the Ameri- n automobile industry and some other industries are taking cond place to Germany and Japan. Here is an instance of great portance to agriculture where the United States can avoid king second place to other countries. But first we must get on ith the research we are well equipped to conduct but are not rsuing for lack of funds.

Four, it is conceivable that BLV virus infection in cattle may adversely affect milk production, fertility, and susceptibility to other diseases. This possibility is based on research in other species where it has been shown that leukemia viruses have significant immunodepressant properties, that is, they reduce the ability of the body to fight infection.

Five, although it appears unlikely that BLV causes leukemia in humans, the available data are not sufficient for a definite conclusion, particularly because of the limited sensitivity of procedures used in attempts to detect BLV in humans.

It should be noted that a large segment of the dairy cattle population is infected with BLV and that many infected cattle release infectious virus or virus-infected lymphocytes in milk.

There is also evidence indicating that BLV is infectious for chimpanzees, infects human cells in tissue cultures, and crosses species barriers under natural conditions. These are compelling reasons for thoroughly investigating the potential of BLV as a human health hazard. Before it can be stated unequivocably that BLV poses no threat to the public health it will be necessary to conduct studies utilizing more sensitive serological, immunological and molecular hybridization techniques.

Whether or not BLV plays a role in the development of human leukemia, the mere fact that a leukemogenic virus is present in cow's milk places our Nation's great dairy industry under a threatening cloud.

The urgent need for expanded BLV research is obvious. It is equally plain that the cost of this research should be shared by the National Cancer Institute and the USDA. NCI justifies its substantial support on the basis that bovine leukemia is an unique animal model system for studies on the cause, pathogenesis and prevention of human leukemia.

Greater support by the USDA can be justified on the basis of the economic importance to the livestock industry of bovine leukemia and bovine leukemia virus infection, and because bovine leukemia infection poses a serious threat to the dairy industry.

At the University of Pennsylvania's comparative leukemia studies unit we are anxious to expand our research in the following areas:

One, the natural mode of transmission of the virus. This must be thoroughly understood before effective control and eradication measures can be developed.

Two, vaccination of cattle to protect them from bovine leukemia virus infection. This is a most promising approach because BLV is transmitted mainly by contact during postnatal life.

Three, the identification of genetic markers which would tell whether an animal is susceptible to BLV infection and to development of leukemia. If we had such markers we could develop herds resistant to BLV infection and/or the leukemogenic effects of BLV.

Four, the effect of BLV on the host immune system.

Five, the effect of BLV on milk production, fertility, and susceptibility to other diseases.

Six, further studies on the biological and antigenic properties of BLV aimed at developing more sensitive, rapid, practical, and inexpensive methods for the detection of BLV.

even, public health implications of BLV. These must be ap-
ached with proper methodology, for example, a highly repre-
tative molecular probe. This should be done in populations fre-
ntly exposed to BLV, for example, in Venezuela humans are
n bitten by insects which have fed on BLV infected cattle.
inally, I do not believe that my scientific colleagues at the
DA really agree, as they have testified, that S. 2043 is a piece of
ecessary legislation. However, I do understand the restraints
ced on civil servants' testimony by their Office of Management
Budget overseers. It is a fact that at the time I prepared this
timony, the Senate Agriculture Committee had not yet heard
n the administration via the Department of Health and Human
vices, either in support of or in opposition to this bill. However,
ave been reliably informed that the National Cancer Institute
forwarded to the Department a recommendation that the au-
rization you are exploring is a needed authorization and one
h which the National Cancer Institute is fully prepared to coop-
te.

hank you.

Mr. DE LA GARZA. Thank you.

Dr. Ferrer, do you have any comments?

Dr. FERRER. No, Mr. Chairman.

The curriculum data of Dr. Marshak is held in the subcommit-
file.]

Mr. DE LA GARZA. Thank you very much. You are invited to
ain and listen to the other witnesses.

Our next witness is Dr. Hernan F. Acevedo, senior scientist,
partment of Laboratory Medicine, Allegheny General Hospital,
tsburgh, Pa. He is accompanied by Dr. John Harshbarger, Direc-
Registry of Tumors in Lower Animals, Smithsonian Institution.
We welcome you and are happy to hear from both of you at this
e.

ATEMENT OF DR. HERNAN F. ACEVEDO, SENIOR SCIENTIST, DEPARTMENT OF LABORATORY MEDICINE, ALLEGHENY GENERAL HOSPITAL, PITTSBURGH, PA.; ACCOMPANIED BY DR. JOHN HARSHBARGER, DIRECTOR OF REGISTRY OF TUMORS IN LOWER ANIMALS, SMITHSONIAN INSTITUTION

Dr. ACEVEDO. Thank you, Mr. Chairman.

Mr. Chairman, and members of the subcommittee, thank you for
opportunity to appear here today in support of S. 2043, the
imal Cancer Research Act.

My comments will be directed mainly to parts (c), (d), and (e) of
bill. I will present a brief summary of the concept of the
stence of a common factor, as mentioned in (d), in the process of
lignant transformation. This theory is based on the following
olished and confirmed observations made in our laboratories.
One, the detection in malignant cells of a material similar to
rigonadotropin, CG, also known as chorionic gonadotropin, the
rmone of pregancy, which is associated with and/or is part of the
mbrane that envelopes the cell, or cell membrane.

Two, that at the present time there are only two normal, the
entific term is "nontransformed" cells in which CG is detected,
trophoblast in the female and the spermatozoa in the male.

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Trophoblasts are cells that appear immediately after conception, one of the two cells of the first division. They multiply rapidly and form a wall around the embryo as part of the placenta. There is strong evidence to support the idea that some of the products synthesized by these cells, mainly CG, are part of the mechanisms that permit the embryo to survive the attack by the immunological system of the mother, thus avoiding rejection.

Three, that this membrane-associated CG-like antigen—and antigen is a material usually of a protein nature that reacts with an antibody—is also expressed in malignant, transformed, cells of all species other than man, that have been studied to date; that is, rat, mouse, hamster, and snake, in vitro, grown in a test tube, and in vivo, in the tissue obtained by surgery or autopsy.

These findings indicate the possibility of the existence of a common biochemical denominator characteristic of the malignant transformation, the long process by which a normal cell changes into a cancer cell that produces disease and kills, irrespective of species and of the way by which the malignant transformation was initiated—carcinogenesis by pollution-chemical compounds, viruses, radiation, and so forth.

Four, that this CG-like antigen is also expressed in the walls or membranes of several strains of different species of bacteria, and,

Five, that, to date, every bacterial strain that expresses the CG-like antigen has always been isolated from a cancer patient—cancer associated bacteria—but not all cancer associated bacteria have the capability to express the CG-like antigen.

The discovery that some strains of different species of bacteria are able to synthesize and express the CG-like antigen appears to be of outstanding significance, not only because it is the first demonstration of the natural synthesis of a human hormone-like product by bacteria, but also because of its biological, physiological, and chemical implications involving the fields of cancer, genetics, bacteriology, molecular biology, and epidemiology.

The demonstration of a high frequency of the existence of CG-producing bacteria, concomitantly with the presence of malignant and/or premalignant conditions, will undoubtedly establish the isolation of the microorganisms and the detection of the CG-like antigen as one of the most useful and sensitive tests for the presence of malignant transformation.

Finally, because of the presence of the CG-like material in the cell membrane of malignant cells, such demonstrations will also enhance the possibility of the development of a specific bacterial vaccine, to be used instead of the nonspecific vaccines like BCG, corynebacterium parvum, and others, that are currently in use as adjuvants in the treatment of cancer. Such vaccine may, perhaps, fulfill the requirements for its use as a preventive vaccine, as the most practical way to avoid the clinical presentation of the disease.

It is obvious that the aforementioned findings and theories can be of the utmost importance, scientifically and practically, if they are extended to domestic animals and wildlife, since the disease we call cancer knows no species barrier, affecting all domestic animals, wildlife and poultry, hotblooded and coldblooded, vertebrates and invertebrates.

Therefore, the need for additional funds to conduct research on animal species other than the usual laboratory experimental animals and to adequately coordinate such basic research as S. 2043 intends, is imperative.

Funds are also needed to perform and/or to extend histopathological and frequency studies in order to obtain the data needed to establish statistical correlations, indispensable for diagnostic, epidemiological, and so forth, type of investigations, and for therapy and preventative, vaccines, trials.

For these reasons, tumor registries need to be initiated and implemented. I was dismayed to hear that there is the possibility that the NCI will discontinue the funding of the registry of tumors in lower animals—invertebrate and coldblooded vertebrate animals—at the National Museum of Natural History, Smithsonian Institution. Its role in the study of environmental carcinogens in aquatic animals was clearly demonstrated at the 1976 meeting on aquatic pollutants and biologic effects with emphasis on neoplasia sponsored by the New York Academy of Sciences.

In respect to this type of information, and its importance, it is of interest to note that Dr. Dale K. Sorensen, chairman of the Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, in his testimony at the Senate hearing mentioned that the occurrence of tumors in cats and dogs, hospitalized in 12 veterinary teaching hospitals in the United States, as reported for a 5-year period, 1964 to 1969, was 5.5 percent, and that malignancy was one of the most important causes of death in dogs.

What to me is more interesting from Dr. Sorensen's testimony is that there appears to be no current or complete statistical information of the disease in pets, animals that play such an important role in our way of life.

Mr. Chairman, members of the subcommittee, I conclude my statement at this point. I consider that Senate bill 2043 is a step in the right direction, and I hope the Congress of the United States will enact this bill.

I am ready to answer any questions from the subcommittee, as well as from any person participating in this hearing.

Again, I thank you for this opportunity.

I will ask the permission of the chairman to show some slides to give you an idea of what we are talking about with respect to the CG antigen. This material is exclusively in animals and not in human beings.

My colleague, Dr. Naughton, has experience in human beings. Dr. Harshbarger will offer some comments with respect to tumors in lower vertebrates.

Mr. DE LA GARZA. Thank you very much, Dr. Acevedo. We appreciate your testimony. Perhaps now we will hear from Dr. Naughton.

Dr. Naughton is professor of obstetrics and gynecology, biophysics and genetics, University of Colorado Medical Center in Denver.

Welcome. You may proceed.

STATEMENT OF DR. MICHAEL A. NAUGHTON, PROFESSOR OF OBSTETRICS AND GYNECOLOGY, BIOPHYSICS AND GENETICS, UNIVERSITY OF COLORADO MEDICAL CENTER, DENVER

Dr. NAUGHTON. Thank you, Mr. Chairman.

I want to address myself to one small portion of this bill and that is the lack of funding for work on human chorionic gonadotropin. I would just like to present a brief case history of my own experience.

In 1973 and 1974, my colleagues and I at the University of Colorado Medical School made the observation that HCG—human chorionic gonadotropin—appeared to be a surface component of a large variety of human tumors as well as a component of the surface of the placenta.

These results were published into two papers. I would like to ask that these be placed in the record at this point.

[The material submitted is held in the subcommittee file.]

Dr. NAUGHTON. The fact that HCG appeared to be a surface component of a variety of tumors, that is, a common marker seemed to us to be an important finding, and we proposed in three different grant requests to the NCI making use of this fact to localized tumors by labeling antibodies to HCG with radioactive iodine.

The antibody would then become attached to the tumor surface and a whole body scan would show areas of radioactivity where the tumor was located. The experiments were to be done in nude mice in which human tumors can be implanted.

All the grants were turned down as being impractical. Yet in June of this year, a paper appeared in the Journal Science using precisely the methods outlined in our grant requests showing that the method did work and, furthermore, the metastasized tumors were found by this method that were not observed by any other known method.

This is just a simple case if you are too early in the field you do not get supported, I think. I think the funding for human chorionic gonadotropin is very important. It does appear to be a common marker. I think it might be a great lead in cancer research, both in humans and in animals.

That concludes my testimony.

Mr. DE LA GARZA. Thank you very much, Dr. Naughton. Dr. Harshbarger?

Dr. HARSHBARGER. Thank you, Mr. Chairman.

I have some slides which I would like to show of lower animal tumors. I would like to explain the benefits of studying lower animal tumors. Dr. Acevedo also has some slides. I would like to leave any comments I have for the slides.

Mr. DE LA GARZA. How long do you think it will take? We have a problem of time.

Dr. ACEVEDO. We can go very fast. Let us say 10 minutes.

Mr. DE LA GARZA. Mr. Wampler, do you have any questions of Dr. Sorensen, Dr. Marshak, and Dr. Ferrer?

Mr. WAMPLER. Not at the moment, Mr. Chairman.

I think the only question I did want to ask is this. It appeared that our export potential in dairy cattle, essentially, was being

seriously restricted because of conditions that were being imposed because of hostile infections.

I was just wondering if you could tell me very quickly what research is being done in other countries in this very vital area? Is it substantial? Could you comment on that very briefly?

Mr. DE LA GARZA. Dr. Sorensen, you touched on that.

Dr. SORENSEN. Dr. Marshak said it.

Dr. MARSHAK. The European Common Market countries have made a commitment of the Common Market to it. In fact, they sponsor every year a very important international meeting of all the Common Market countries to which we are invited.

It is the only international meeting of its kind on bovine leukosis. Every one of the European Common Market countries have major research programs on bovine leukemia. They are far ahead of us in terms of the relative investment in funds and manpower.

Mr. WAMPLER. Do they share with you the results of their investigations?

Dr. MARSHAK. Yes; the sharing is not only done at meetings, but, of course, through the publications and journals.

Mr. DE LA GARZA. I wanted to verify a number. One of you gentlemen mentioned that 30 percent of the American herd is infected with leukemia.

Dr. MARSHAK. Yes; it is reliably estimated that upon the number of studies done, approximately 30 percent of the dairy cattle population of the United States is infected with the virus, and 60 percent of the herds are infected.

Mr. DE LA GARZA. It is 30 percent of the dairy cattle and 60 percent of the U.S. herd?

Dr. MARSHAK. That is right.

Mr. DE LA GARZA. That means if a foreign country has a restriction either from positive infection or coming from an infected herd, it could reduce your export by 60 percent?

Dr. MARSHAK. It is reducing it very appreciably. I did not attribute the quote I made about this being the largest threat to our export business. It comes from the head of the international division of the Holstein Association.

Every week or so an organization or farmer will call me and say: "We have this bull that we have just sold for $50,000. He is BLV positive and we cannot ship him. Is there anything we can do about it?"

The answer is no, there is nothing you can do about it because once an animal is infected, for all practical purposes it is infected for life.

Mr. DE LA GARZA. We thank you, Dr. Sorensen, Dr. Marshak, and Dr. Ferrer. We invite you to stay if you care to. But if you need to depart, we will not ask you to stay for the slide presentation.

We will proceed now to the slide presentation.

Dr. ACEVEDO. At this very moment I would like to clarify a couple of concepts. We look at the vaccine against Marek's disease. In reality what you have is a vaccine against the virus. You do not have a vaccine against cancer. Vaccines are used in a specific type of transformation which the agent has been proven, that is, the inducer.

Vaccines are being used in cancer patients but those vaccines are known as specific. What they do is stimulate the defense in general. When my colleagues and I are talking about the possibility of the vaccine in this case, it will prepare the animal or the human being to elaborate the antibodies against the hormone.

It will attack the cancer cell itself by the effect, the destructive effect it will have at the layer of the cell membrane.

So, it will mainly be a preventative vaccine. It will avoid the proliferation of the cell by killing the cells and, in that way, avoid the transformation.

One concept that has to be clear is the process of malignant transformation which at this moment is in every one of us. It is part of life. We cannot avoid it.

The techniques we use are very modern techniques. They are based on the depiction of the localization of the material in the cells itself.

If it is in one cell present, we can see it. The sensitivity of these methods goes to the level that we can see by light microscopy some membranes if it is present.

When we look at the electron microscopy use in the procedures we can detect 7 to 10 molecules. Here you have the typical trophoblast. This is the reaction.

Here we have the normal spermatozoa. He has to defend itself because it is a foreign body in a body of a woman. Therefore, it does because every cell carries the formation to synthesize this product. We were the first to demonstrate this. This is one of the ways that the spermatozoa survives in a foreign body.

These are the types of cells in animals that we have studied, different model animal tumors in which we have tumors that are promoted by chemicals. These are called tissue culture cells. They are isolated cells.

This is a list of in vivo studies in animal tumors again of every type and the different types of neoplasms as well as others that we have studied.

Here is the identification.

Here we have cells of those animal tumors showing what reaction CG has. When you inject the cells you transplant the cells into a given experimental animal. It kills the animal within 3 days, 100 percent of them.

You see the material is totally in the membrane in the whole cell. These cells are unfixed cells.

When you look at the other reaction it shows it here.

When you look by electron microposopy, you see that the cell has all the material in the cell membrane.

You can see here we have another animal. It is a sarcoma. The sarcoma shows the characteristics. It is a tissue culture. Here you have the control.

This now is a malignant tumor in tissue culture. The snake cell also produces the same type of compound that we believe characteristic of species.

Here we have microbes, bacteria. These bacteria have been isolated from a cancer patient.

When we look at the bacteria that synthesizes the CG, it does not follow the normal ways.

We have bacteria that at the same time multiplies two times, three times, four times, five times, six times.

We can see that the cells are different. We have found all those zones that are indicated by the arrows that differs it from the normal bacteria that does not produce the hormone.

Here we have another bacteria that is divided in a completely different way. In place of dividing itself, it is multiplying like fungus. You can see it here coming from one side of the bacteria. You have two there or three. Then the new is free and comes out here and grows and grows. This is characteristic of these bizarre forms of bacteria.

Here you have another bacteria. This is isolated from a patient that has carcinoma of the colon. You can more or less see the normal one on the side. The big one is the same, but this one is producing CG and in the process of division, in place of dividing it in two, it has elongated itself and is going to be dividing into five new bacteria. This characteristic is seen here.

Here you have the ecolyte, one of the most common bacteria. It is situated here covering the two cell membranes of the wall of the bacteria.

The fact that these bacteria are mutants and divide themselves in the form I have shown leads us to believe that these bacteria can respond to forms that have not been very well studied.

These bacteria are parasites that live inside the cells. We call them revertants. There are people at Tulane doing work in that.

So for the very first time we have an association that could be of tremendous importance. This association is found in that compound that we call CG.

Thank you very much.

Mr. DE LA GARZA. Thank you very much, Dr. Acevedo. We appreciate you and the other witnesses very much.

It has been very interesting and very educational for us. For that we thank you.

That will be all the testimony.

We think we should continue the hearing and invite witnesses related to the human part of cancer and have some testimony from them so that we might in ourselves coordinate the legislative history to the extent that we can move expeditiously with this legislation.

Did you have a further statement, Dr. Harshbarger?

Dr. HARSHBARGER. I have some slides that I could show for a few minutes if you will take a few more minutes.

Mr. DE LA GARZA. Yes, sir. I apologize. I thought those were all the slides.

Dr. HARSHBARGER. I am a Ph. D. pathobiologist. I am Director of the Registry of Tumors in Lower Animals at the Smithsonian which was established about 14 years ago by funding by the Cancer Institute.

The purpose of this was to look at all the other 99 percent of the animals of the world other than mammals and birds to see if they have cancer and where the cancer is and what forms it takes.

The Tumor Registry acts as a specimen depository, as a diagnostic center, as an information center, and as a research group. We

have five people. One of them is supported by the Food and Drug Administration rather than the Cancer Institute.

There are very few people interested in tumors in coldblooded animals. On my mailing list are about 1,200 people. I know virtually every person who is doing any work or has an interest in this area.

I get specimens from all over the world, from polluted habitats, from experimental labs, from fishermen, from commercial people. They want diagnoses. They want to know if it is significant. I write them letters telling them.

We have computerized all the information so that we can go back in the literature or in the specimen file and see what is available.

Neoplasms have been found in all the coldblooded vertebrates which include reptiles, amphibians, fish, sharks and rays, and the jawless fish like lampreys. It also has been found in insects. We have one case in a flatwork which is pretty good. We think that all the other possible cases that have been reported in the literature cannot be verified.

So those are the only ones we accept and verify.

Some of the benefits that people use when they are setting up the Registry—rather, there are some animals that do not get cancer and if not, why not? Is there an antitumor agent that could be extracted?

As you may know, half the chemicals that are used for cancer therapy are from a natural origin.

Another thing was simpler systems. The invertebrates do not form antibodies. So, if you were studying cancer in the simpler system, it would be analogous to learning how to fly by first going up in a simple Cessna 150 rather than being put into a sophisticated machine, like a multiengine jet.

But there are other potential benefits. I will show a few slides just to illustrate some of these. I will go as fast as possible.

One benefit would be to protect endangered and commercial species. This is a green sea turtle. You can see on its head it has some lesions. I show this blowup. You can see tumors in this turtle. These are not malignant cancers, but they definitely can impair the turtle's competitive ability to get along in his environment. This is an endangered species. It is also a commercial species.

Tumors occur in salmon. This one was from Lake Michigan.

Here is one from the west coast. This is a salmon. This is a tooth-bearing tumor. It is actually a cancer. People get this cancer.

These are commercial animals. In the Great Lakes, 80 percent of salmon in Lake Erie have thyroid goiters. Some of them can become carcinomas.

Here is an oyster. Out to the left you can see some grape-looking clumps. That is a tumor. If you look at the histology, you can see the tumor growing. It is from the mantle. It is the cells that ordinarily would produce the cells that are producing this big growth.

If you look at it at a higher power you can see all the black areas where the cells are dividing. It is a rapidly growing neoplasm.

This is a frog. You see the two lumps in the back. Those are the kidneys that have a carcinoma. When you look at the kidney, you

can see these bizarre tubals. When you look at it at a higher power, you see some very dark inclusions. Those inclusions contain herpes virus. The study of cancer in this frog yielded the first evidence that a herpes virus might be a tumor virus. So, a possible benefit of studying tumors in lower animals is to find new tumor viruses.

Another possible benefit would be to find new chemical carcinogens. This is a poor picture of a rainbow trout that has a liver tumor. On the inside you can see nodules on the tumor.

This picture from "Cancer Research" was honoring the man on the right who studied cancer in rainbow trout. In about 1960 they changed the trout feed from an animal base feed to a grain base feed. That coincided with the time that the cancer started developing.

The people on the left were studying the outbreak of poultry toxicosis in England. They traced that toxicosis to aflatoxin or contaminants in the feed by mold. It was really this gentleman who made the connection with cancer. They were eating moldy food, too. They were getting cancer.

So the combination of these people showed that aflatoxin was a real potent carcinogen.

There is a lot more to that study which I would like to go into, but I cannot for lack of time.

I would like to say that lower animals can be used as good test animals for screening chemicals. Rainbow trout might be an especially good one. One nice advantage of the animal like the trout versus mouse experiments is that there is a precise end point. It is not a thing that trout never get tumors unless they are exposed to chemicals. They have been treated with a lot of chemicals. So they either get them or they do not know the chemical is a carcinogen or not. You do not have to do statistics with the control group to determine that.

Trout and other fish also get another kidney tumor which is one of the most common solid tumors in people. This might point out that lower animals could be useful as models for studying tumors in higher animals.

There is a polluted lake on an Air Force base in Texas where 50 percent of the salamanders get skin cancers of different kinds. We have reason to believe that there is a chemical that is in this pond that is causing the tumors in the salamanders.

The point of it is that lower animals can be indicative of carcinogens in the environment. We have a lot of evidence of that.

Surveying lower animals might contribute to that.

Insects get cancer. This is the best known animal so far as genetics is concerned. It has been worked out better. Large genetic studies are done. This animal has 16 specific neoplasms that can be pinpointed to a specific locust on a specific chromosome.

I do not know where you could find a better model to study the genetic influence of cancer than this.

There is a good example in fish, too, that could be used for the same purpose.

I would like to point out the possible benefit of studying lower animals is what I call fallout.

We were studying tumors in clams and oysters from the Chesapeake Bay as a result of interest by the FDA.

In the process of studying these tumors, we saw these inclusions in some of these cells. So we looked at them with the electron microscope. They turned out to be organisms like chlamydia which occurs at the level between the bacteria and viruses. That can cause a lot of diseases in farm animals and people, including something atypical of a pneumonia-like disease.

This was a chlamydia and for the first time ever it had its own virus disease. That is what those little dots are inside the bigger ones. So for the first time we found a chlamydia.

In studying tumors we ended up finding that a bivalve mollusk can be a host for a group of organisms that had medical significance and nobody knew it was there.

The Food and Drug Administration is concerned.

I would like to make a plug that there are a lot of potential benefits to studying tumors in the lower animals as well as the higher ones.

Thank you.

Mr. DE LA GARZA. Thank you very much. We might need to spend about a day with you down the line, perhaps after we dispose of this legislation, hopefully successfully.

Dr. HARSHBARGER. You are welcome to visit me at the Smithsonian anytime. I will show you the real specimens.

Mr. DE LA GARZA. Thank you and the rest of the witnesses.

I would like to insert in the record a copy of Dr. Netterberg's report, "The Road Not Taken: Toward A Cancer Vaccine."

Without objection, so ordered.

[The publication referred to is held in the subcommittee file.]

Mr. DE LA GARZA. The committee will stand in recess subject to the call of the Chair.

[Whereupon, at 12:42 p.m., the subcommittee was recessed.]

ANIMAL CANCER RESEARCH ACT

THURSDAY, SEPTEMBER 4, 1980

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON DEPARTMENT INVESTIGATIONS,
OVERSIGHT, AND RESEARCH OF THE
COMMITTEE ON AGRICULTURE,
Washington, D.C.

The subcommittee met, pursuant to notice, at 10:10 a.m., in room 1301, Longworth House Office Building, Hon. E de la Garza (chairman of the subcommittee) presiding.

Present: Representatives Skelton, Glickman, and Wampler.

Staff present: Robert M. Bor, chief counsel; John E. Hogan, counsel; J. Robert Franks, associate counsel; Glenda Temple, clerk; Mario Costillo, Gerald Jorgensen, Thomas Adams, Anita Brown, Bernard Brenner, and Mori Irvine.

Mr. DE LA GARZA. The subcommittee will be in order.

I have been asked if Dr. John Potter could be heard first as he has to return to the hospital. I would ask if the other witnesses have any objection to that or if there is any problem timewise, so we could accommodate Dr. Potter. If I do not hear any, we will continue with the consideration of S. 2043, the Animal Cancer Research Act.

We welcome all of you. We appreciate your attendance and your cooperation in this respect.

We will hear from Dr. Potter first.

STATEMENT OF DR. JOHN F. POTTER, DIRECTOR, VINCENT T. LOMBARDI CANCER RESEARCH CENTER, GEORGETOWN UNIVERSITY, WASHINGTON, D.C.

Dr. POTTER. Mr. Chairman and members of the subcommittee, I am delighted to be able to come before you today to present an account of the progress which is being made in the diagnosis and treatment of cancer. This progress has come about as the result of a national commitment to cancer research.

The scope of cancer is known to all of us. One of four Americans will live to develop an aggressive form of the disease. It will afflict 56 million Americans who are now living. In addition, cancer will strike in approximately two of three families in this country. In the 1970's, there were an estimated 3.5 million cancer deaths, and over 6.5 million new cancer cases developed. Certainly, the magnitude of the cancer problem is readily apparent.

In addition to these statistics which recite only the occurrence rates of cancer, the emotional impact of this disease must not be forgotten. No disease can strike terror into the heart of its victim as does cancer. The emotional suffering which the disease produces

is probably unique among all of the ailments which afflict mankind.

In addition to emotional suffering, the physical suffering which the disease causes is also well known. I think it is safe to say that cancer has become the scourge of mankind in the later years of the 20th century.

Even though the occurrence rate of cancer is increasing and the death rate is increasing slightly, there are highly encouraging developments which have taken place in cancer research in the last few years. For example, only about two decades ago, at about the time that I was beginning my professional involvement with cancer, all children who developed acute leukemia died of this disease.

Wilm's tumor is a cancer arising in the kidney which afflicts young children. Only a little over two decades ago, only about 15 percent of these children could be cured. As a result of intensive investigation of the utilization of surgery, irradiation therapy, and chemotherapy, more than 80 percent of such children are now saved. Treatment has become so effective, and cure rates so good, that refinements are being evaluated to see how much this aggressive treatment can be cut back.

I can remember distinctly at this time, I was a surgeon on the surgical branch of the National Cancer Institute, and among our duties from time to time was to come down and do consultation work on the pediatric ward in the National Cancer Institute where almost all of the children present were sufferers from leukemia. I can recall very vividly all these little children—20 or 30 or so on the ward—riding around on their little tricycles and so forth. It was always a striking feeling for us, as surgeons, to walk on this ward because we knew, in looking around, that all of these little children would die of their disease.

As a result of very intensive clinical and basic investigation in the last two decades, this situation has profoundly changed. As a result of the development of new drugs, awareness of how these drugs can be used more effectively in combination, utilization of antibiotics, and platelet transfusions, clinical scientists have now progressed to the point where over 50 percent of these children will go into remission, that is, will be expected to be cured of their disease.

I think this is a very graphic illustration—at least to me personally—of the progress which cancer research has made in just the span of two decades.

There are other examples which are also quite impressive to me, Mr. Chairman. Again, in the late 1950's, as a surgeon at the National Cancer Institute, I was called upon to operate on young women with chorio carcinoma of the uterus. It is a rare tumor, fortunately. It arises from the products of conception.

In those days, really the only effective treatment for this condition was a surgical operation in which the uterus, the tubes, and the ovaries would be removed. Unfortunately, all too often, Mr. Chairman, this could not be done because the disease had already extended locally or to a distant spot, such as the lungs, so that these patients could not be treated with expectation of cure.

As a result of investigation into the chemotherapeutic utilization of drugs for this disease, this condition has now undergone a truly dramatic improvement. At the present time, most of these women will be cured; and, furthermore, they will be cured without a surgical operation which sterilizes them. In other words, they can now be rid of this grim cancer—or what used to be a grim cancer—with preservation of childbearing function. I think this is a very impressive testimonial to what cancer research has achieved in a relatively short period of time.

Testicular cancer—a form of cancer which frequently occurs in young males—also can now be treated with much greater effectiveness than during the period of time just a few years ago. As a result of what we call multidisciplinary treatment—the utilization of surgery, of irradiation, and multiple drug chemotherapy—young men who formerly would have died of testicular cancer are now being cured of this condition.

Our scientists and clinicians at the Lombardi Center at Georgetown University have, I believe, contributed to this national war on cancer, and I must say that we are very much indebted to the Federal Government and to the National Cancer Institute for the partial but extensive support which it has given to our cancer research and treatment activities.

To mention a few examples of current research at the Lombardi Center, I would like to call attention to our breast cancer screening clinic which has been in operation for approximately 10 years. This clinic is dedicated to the detection of breast cancer in women at the earliest possible stage of the tumor's development. Since breast cancer is far and away the most common form of cancer in the female, a project of this type is clearly very important; 10,000 women who had no symptoms of a breast tumor were screened by physical examination and by X-ray mammography; a total of 117 cancers were detected in this population. What is of most interest is that when women who had these cancers detected in this screening program came to surgery, only 18 percent of them had cancer which had spread to the regional axillary lymph nodes. This is in sharp contrast to women who came to surgery after they had noted the tumor themselves or it had been detected by a physician in a routine examination. These women who do not have the benefits of an early screening program have approximately 47 percent of their nodes positive.

One of the most significant determinants of the patient's prognosis is the presence or absence of axillary metastases, so it is clear that the outlook for these women has been markedly improved as a result of a clinical research screening program.

Our medical oncologists at the Lombardi Center have contributed substantially to the development of new drugs and the utilizations of more effective combinations of chemotherapeutic drugs. These investigators have developed the so-called FAM protocol for gastric cancer. This consists of the utilization of 5-fluorouracil, adriamycin, and mitomycin C. This has become one of the most effective forms of treating metastatic cancer of the stomach.

In addition, a new drug, chlorozotocin, was developed in large part at our center. This agent has significant anticancer effects without the production of bone marrow toxicity.

Our center also has a strong interest in immunologic oncology. This area, which could pay big therapeutic dividends in the future, seeks to find ways of detecting early cancer by immunologic means and to stimulate the natural resistance of the body to the development and spread of cancer.

As you may know, Mr. Chairman, the Lombardi Center works collaboratively with Howard University Cancer Center in many areas of cancer research. Among these is the utilization of intraoperative irradiation therapy for locally advanced cancers. Surgeons of the Lombardi Center operate on their patients in coordination with their colleagues at the Howard University Hospital in a specially designed and highly sophisticated operating room which contains a linear accelerator X-ray machine. These surgeons have operated on patients with locally advanced cancers of the cervix and the pancreas. When the organ is exposed, direct irradiation of the tumor through the open abdominal wall is performed.

I think you would agree with me that a sophisticated facility of this type and the types of highly competent clinicians necessary from both the surgical viewpoint and the irradiation therapy viewpoint to carry this out have come about primarily as a result, I believe, of governmental support of cancer research in this country.

Our epidemiologists have also worked in collaboration with their confreres at Howard in documenting the high incidence of cancer in the Washington, D.C., area. It comes as a surprise to many that Washington, D.C., has the highest cancer incidence in the United States. The city of Baltimore, Md., only 40 or so miles away, has the second highest incidence of cancer in this country. This, we believe, is due primarily to the very high incidence of cancer in blacks and especially in the black male.

Our epidemiologists, working in collaboration with their confreres at Howard University, are attacking the very important problem of what are the specific causes for this high incidence of cancer in the black male.

Mr. Chairman, I have briefly presented some of the advances which have been made in the control of cancer as a result of clinical research. Unfortunately, much still remains to be done, and we have barely scratched the surface of understanding of this biologic enigma which so disastrously afflicts the American people.

As a clinician, I am aware of how important this struggle is. I am also aware of the vital role which the Congress of the United States has played in funding cancer research endeavors and, in specific, in the funding of cancer research centers such as the Lombardi Center.

I appeal to you and to your colleagues to continue this support, without which cancer research can proceed no further. We have made substantial strides forward in cancer treatment; not only cancer scientists but, Mr. Chairman, much more importantly, their cancer patients and the American people are deeply indebted to the Congress for its wisdom and compassion in supporting the struggle against cancer.

Thank you.

Mr. DE LA GARZA. Thank you very much, Dr. Potter.

Mr. Wampler?

Mr. WAMPLER. Thank you, Mr. Chairman.

Dr. Potter, we thank you very much for your presence here this morning and for a very fine statement, particularly advising the subcommittee of the progress that is being made at the Lombardi Cancer Research Center of Georgetown University here in Washington, D.C.

As you know, the purpose of these hearings is to consider the bill, S. 2043, which would provide for research and coordination of research and the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife.

While this committee does not normally have jurisdiction over the subject matter of research in cancer as a whole—that rests in other committees of the Congress—we are extremely interested in this basic field of research affecting domestic animals and poultry.

If I correctly interpreted the thrust of your testimony, it was that, as far as the Congress and the Federal Government are concerned, we need to continue our efforts in all areas of cancer research. It is not the purpose of this bill to detract from ongoing efforts but simply as a way of attacking a different form of cancer so that we can take this valuable information of research into animals and, hopefully, relate it to the causes of cancer in human beings.

Would you agree that this bill will be important in the overall approach to cancer research?

Dr. POTTER. Yes, I would, Mr. Wampler.

As you know, I am a clinician, so I spoke primarily from the point of view of clinical cancer. Nevertheless, it would appear to me that investigation of cancer in domestic animals would also be of importance.

As a generalization, biologic phenomena do not differ extraordinarily across species lines. Therefore, it would seem to me that information discovered about cancer in animals could well—no guarantees, obviously—play a beneficial role in learning something about how human cancers develop.

There is also, of course, speculation that possibly the two may be related—that factors may cross species lines from cancer in an animal and may somehow or another be involved with human cancers. My copanelists today are much more expert in that than I, and I will leave further testimony to them. But certainly I think, in answer to your question, it is important to support cancer research in these animals.

Mr. WAMPLER. Earlier witnesses testified to the rather remarkable progress that had been made in immunization against certain types of viruses, especially in poultry. This is an area that has always rather intrigued me.

Under the provisions of the bill before us, the authorization and any subsequent appropriation would basically be under the administration of the Department of Agriculture but with full consultation and coordination with the National Cancer Institute and other agencies of the Government so that we do not have a duplication of effort and that there be a full exchange of data and information to be utilized to the maximum degree.

So, on that basis, you certainly have no objection to this bill at all, do you?

Dr. POTTER. No, none at all.

Mr. WAMPLER. Thank you very much, and thank you again for your time and for the work that you and your colleagues are doing.

Mr. DE LA GARZA. Mr. Skelton?

Mr. SKELTON. I have no questions, Mr. Chairman.

Mr. DE LA GARZA. Mr. Glickman?

Mr. GLICKMAN. No questions, Mr. Chairman.

Mr. DE LA GARZA. Doctor, as Mr. Wampler told you, the hearings are on S. 2043.

We called this meeting today, in part, to see if there is some degree of cooperation, at least in your area, to your knowledge, with the research being done, on the one hand, on domestic animals and fowl, for that basic reason, and to what extent, to your knowledge, in your area is there coordination as far as research data are concerned that could be utilized in humans or vice versa.

Dr. POTTER. Certainly, Mr. Chairman, the information that is obtained and is published in essentially veterinarian types of publications does become known to the medical community, and, of course, this is a highly beneficial thing because some leads can be developed which might, in the future, play an important role in clinical research or in research a little more closely directed to the patient.

I cannot say that at the present time we have any close relationship with veterinarian types of research at our own institution. Nevertheless, I would not want to minimize the possibility for a potential exchange of useful ideas in the future from this sort of a source. I think, therefore, it has a potential for benefit.

Mr. DE LA GARZA. The idea struck us because of Marek's disease in poultry. They have found a vaccine.

Dr. POTTER. Yes.

Mr. DE LA GARZA. I know there is no relationship at all between what could conceivably affect poultry and the human. But you mentioned the similarity of the cancer-causing—I do not know what you would call them.

Dr. POTTER. Obviously, there are these viral diseases in veterinarian animals that do cause leukemia. One of my copanelists today, Dr. Rauscher, of course, is highly expert in this field and received the ultimate scientific accolade of having a virus named after him, so I think that, in the interests of saving the subcommittee's time, I will allow you to refer those questions to the expert.

Mr. DE LA GARZA. Thank you very much, sir.

Those of us who followed the life of Vince Lombardi are very happy to see this great individual's name linked to trying to eradicate the disease which claimed his life so early. I had the privilege of serving twice as Cancer Crusade chairman for my congressional district and had the honor of meeting his son who attends most of the national meetings and participates. We followed his life and his career, with the exception of when they took on the Dallas Cowboys.

We thank you very much for being here, and we appreciate your cooperation.

Dr. POTTER. Thank you, Mr. Chairman.

Mr. DE LA GARZA. We will now continue with the order of the witness list as set out in the call of the subcommittee. So our next

witness is Dr. Vincent T. DeVita, Director, National Cancer Institute, National Institutes of Health.

We welcome you, Doctor, and would be happy to hear from you at this time.

STATEMENT OF DR. VINCENT T. DeVITA, JR., DIRECTOR, NATIONAL CANCER INSTITUTE, NATIONAL INSTITUTES OF HEALTH

Dr. DEVITA. Thank you, Mr. Chairman and members of the subcommittee.

I am pleased to have the opportunity to discuss the programs of the National Cancer Institute. The National Cancer Institute was created in 1937 by an act of Congress and was the first of the 11 institutes at the NIH. We were charged to be the principal Federal agency to research the problem of cancer in humans.

The National Cancer Act passed in 1971 increased our support and gave us responsibility for planning a national and international effort on cancer, and what has resulted is a coordinated international research effort which includes cancer centers throughout the country, one of which, in Georgetown, you have just heard about, which are charged with coordinating the laboratory basic research with the clinical side of cancer and to provide access to cancer care for patients around the country. It provides for support of basic research. Almost half of our budget goes out to support research supported under the grant system. It provides for training, control, outreach programs, and an increasingly important international program on epidemiology which I will return to in a moment.

Our budget can be divided roughly into thirds: one-third on cause and prevention research; one-third on basic and clinical research in treatment; and one-third on research and detection diagnosis, biology, and immunology.

I would like to make a few comments first about the cause and prevention programs. We do believe that most cancers are, in fact, caused by environmental factors. These factors would be chemicals in the environment, biological materials like viruses and fungal products, and also—a very important category—lifestyle, like smoking, what we eat, what we drink, what we do to ourselves. If this is true, then cancer should be a preventable disease if we can find ways to remove these influences from the environment.

In reference to chemicals, we have developed three areas that, I think, are important and worthy of mention. First, in our epidemiology programs which were developed under the increased funding of the Cancer Act, we have begun to plot the incidence of cancer around the country in the series of cancer maps that have been developed on a community basis. These maps identify "'hot spots" that allow us to go in and search for chemicals that might be causing cancer, and we have found some.

We are working, and have worked, to prevent the entry of chemicals that might cause cancer in the environment, and this was developed under a chemical testing program by the National Cancer Institute which has emanated into the National Toxicology Program now run jointly by several institutes of the NIH and other Federal agencies.

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Basic research in this area has come up with rather exciting data on a dual mechanism for the causation of cancer by chemicals called the initiator-promoter theory where there are certain chemicals that can initiate a cancer if they are coupled with a "'promoter." The exciting part of this observation is that many of the influences in our environment, for example, chemicals and cigarette smoke, appear to be promoters. When one removes promoters, one can decrease the incidence of cancer somewhat faster than removing initiators.

In biological areas, we now understand more fully the complex role that viruses play in the causation of human cancer and consider them a risk factor. Although in some cases they appear to be associated with the incidence of cancer in humans, they, by themselves, are not sufficient to cause cancer. This program actually interfaces with animal research, and I would like to return to it in a moment.

Under lifestyles, we have started programs in applied prevention to decrease the incidence of smoking in this country and, in fact, in conjunction with our colleagues in the American Cancer Society, I think we can be proud of the fact that some 29 million Americans have already stopped smoking.

We have some exciting new leads in diet and nutrition that lead us to believe that we can exploit these to alter diet and alter the influence of diet on cancer incidence.

I would like to turn to the second third of the budget, cancer treatment. Dr. Potter told you that up through the 1950's all we had to treat cancer were surgery and radiotherapy, and the equipment and the procedures were crude. Nonetheless, from 1900 to 1930, we could increase the cure rate for cancer to about 30 percent of all serious cancers. Those who were not cured died of circulating cancer cells, and that is still true today.

We needed drugs which, like antibiotics, could cure cancer. The NCI developed a drug development program to provide these drugs and has been responsible in some way for every one of the anticancer drugs that are now available to treat patients, and there are some 30 in number.

We spent much of our time in the late 1960's and early 1970's, after the passage of the Cancer Act, trying to find the answer to the question of whether drugs, by themselves, could cure cancer because this answer would have an important impact on how we approach the research problem for cancer in the 1980's. The answer, I am pleased to tell you, is a clear yes. We also spent time refining the radiotherapy equipment which is now much improved.

While these efforts worked, and they worked initially in cancer of the young, and we are now seeing on a nationwide basis a decrease in cancer mortality under the age of 45, the resources of the National Cancer Act in 1971 allowed us to apply these results in the more common visceral cancers of humans, and, in fact, we are now beginning to see positive results in such common cancers as breast cancer where all the study populations are not only showing a decreased recurrence after surgery when drugs are used but also decreased mortality. Since there are over 100,000 women in this country who get breast cancer, this should have a significant impact. In fact, we are now beginning to see a decrease in the

mortality from cancer in this country below the age of 55 where 25 percent of all the cancers occur.

We now believe that about 41 percent of all serious cancers can be cured by existing methods of treatment. We also have noted in the past decade that the morbidity of cancer treatment, which is significant, is decreasing. In patients who develop a kind of cancer called the sarcomas, we are now able to prolong their lives and cure a significant fraction without taking their limbs as we used to years ago with surgery alone.

There are other new and exciting developments in treatment. The biological development program is just beginning in the Cancer Institute and will be responsible for bringing interferon into clinical trial; there are the new forms of X-ray equipment that will allow us to develop X-ray beams that can deliver precise X-ray to just the tumor and spare the normal tissue; there are drugs that sensitize the tissue to radiotherapy; these are all on the horizon.

The other third of the budget is in detection, diagnosis, biology, and immunology, and the research funds that have gone into these areas have led to many of the exciting things you read about daily in the newspaper: DNA recombinant, methodology that allows us to insert genes into bacteria and turn bacteria into factories; a technique called hybridomas which allows us to produce very pure antibodies that will serve not only for diagnostic testing but, in fact, perhaps for therapeutic approaches in the future.

Altogether, the research support provided by the Cancer Institute and the other Institutes at NIH has produced an astonishing explosion in technology in the biologic sciences.

I would like to turn, just for a moment, to the issue of research in domestic animals. While the NCI's mission is to decrease the cancer burden in humans, causation in animals, as Dr. Potter indicated, is likely to be similar, and animals, in fact, do serve as models for humans, and they can benefit from the research as well.

In the past 15 years, quite apart from its use of animals in basic research, the National Cancer Institute has spent well over $100 million on targeted programs alone in cancer research on pets and farm animals. In fact, our current annual budget for research in pets and farm animals is $18.7 million, which includes 27 grants to veterinary schools.

Our efforts in this area can be separated approximately into three phases. In the early phase, we look for clusters of cancers in humans and animals. The second phase grew out of our frustration developed in the early phase because of a lack of a systematic nomenclature for cancers in animals. The NIC was responsible for the development of a standard nomenclature for veterinary diseases and operations which, by the mid-1970's, was adopted by 20 of the 23 veterinary schools in this country.

We also developed the automated medical records system to support these studies and are about to publish the most comprehensive atlas in the world on tumors of domestic animals.

Having done this, we entered the third phase, which, with this data base, allowed us to do studies on trends in cancers in animals that breathe the same air and drink the same water that we do. We look for common ideologic associations, and we have found

some; for example, bladder cancer in dogs occurs in the same regions where there is a high density of bladder cancer in humans.

We have extended these observations to our international program and have some very exciting leads to follow in the Chinese population where the incidence of esophageal cancer parallels cancer of the gullet in chickens.

We continue to look for associations of cancer in veterinarians, poultry workers, and dairy farmers, and pet owners.

Viruses in cancer are a special program. Our earliest efforts in the special virus cancer program were on the bovine leukemia virus. In fact, the National Cancer Institute has been the major supporter of research on this very important problem in domestic animals and has spent over $25 million on this particular problem alone. We now know, and suspected early in the 1960's, that bovine leukemia and lymphosarcoma was caused by a virus.

The NCI established the facilities for isolating infected herds and laboratories to study them in veterinary schools in Pennsylvania, Michigan, Minnesota, and California in the mid and late 1960's. These laboratories were responsible for working out the infectious nature and the transmission of this virus in cows and in other animals, and they also developed the diagnostic tests that are in use today to identify animals with this illness.

We also surveyed blood samples in thousands of cattle handlers looking for evidence of antibodies that might indicate that the virus could be transmitted to humans and found none. We showed that pasteurization inactivated the virus, and therefore virus in cow's milk was not a public health hazard. We continue to do studies to characterize this virus. We find that it is a very ancient virus; it has very little relatedness to any other virus or any human genetic material, and we have lessons to learn from bovine leukemia.

We did similar studies on the cat leukemia which we now believe is caused by a virus again and, again, have found no associations between owners of cats and cats with leukemia. In fact, the National Cancer Institute virus program has turned up no evidence that animal viruses cause cancer in humans. And, in fact, there is no human cancer at the present time that is known to be caused solely by a virus, which accounts for some of the differences in our approach between animal and human cancers.

There are other examples of our involvement with domestic animals, for example, the cancer eye, a problem that occurs in Hereford dairy cattle. This is caused by exposure to ultraviolet light as some skin cancers are in humans. NCI immunologists have used this model to help develop approaches to the immunotherapy of cancer by injecting vaccines into the tumor that stimulate the response of the host to reject the tumor. The injection of a tuberculosis vaccine into the cancer eye tumor in cattle, in fact, has served as a rather good way to treat this tumor and is of value to the cattle industry. We have also applied this approach to the treatment of skin cancers in humans, particularly one version of a very virulent skin cancer, malignant melanoma, and it is now the most effective way of treating the localized recurrent form of this disease.

Mr. Chairman, these are a few examples of what I think is a demonstration of the National Cancer Institute's interest in the problem of cancer in domestic animals, and we continue to remain interested.

There are major differences in how ideologic agents work in animals compared to humans, largely because of the inbred nature of most of the domestic animals compared to the outbred nature of humans. Therefore, the problem in humans is somewhat more complex. Nonetheless, we will continue to use domestic animals as models for and sentinels for the cancer problem in humans.

Mr. Chairman, this concludes my statement. I will be pleased to answer questions from members of the subcommittee.

Mr. DE LA GARZA. Thank you very much, Doctor.

Without objection, your prepared statement will be included in the record at the conclusion of the testimony.

Mr. DE LA GARZA. Mr. Wampler?

Mr. WAMPLER. Thank you, Mr. Chairman.

Dr. DeVita, I want to thank you for your very fine statement and for your taking time to come and share your testimony with us this morning.

I was particularly impressed with the last paragraph of your prepared statement on page 6. You said, among other things, "By trying to learn more about human cancer, we also learn more about cancer in animals. Though we do not fully understand the causes of cancer, I would be very surprised that we find a major difference in the mechanism of these diseases between man and his companion animals."

I certainly agree with that statement. I have long held that view. Earlier witnesses before the subcommittee expressed concern about the denial of applications for research funds by the National Cancer Institute to certain programs affecting research on animals. I do not say this critically; I realize you operate with a restricted budget. What is your budget for fiscal year 1980?

Dr. DEVITA. For fiscal year 1980, it is $1 billion, Mr. Wampler.

Mr. WAMPLER. I am sure that you have far more requests for funds than you are actually able to honor and to grant. Is that correct?

Dr. DEVITA. About 60 percent of our approved grant applications are not able to be funded. This year we are funding just under 40 percent of approved applications.

Mr. WAMPLER. You, of course, I am sure have read the act that is before us and what is contemplated. Let me refresh your memory on the findings under section 2. Among other things, under (e), it says, "research on diagnosis, prevention, and control of cancer in animals and birds will be beneficial in identifying any common factors in human and animal malignant tumors, if such exist." Do you agree with that finding?

Dr. DEVITA. Yes, sir, I do.

Mr. WAMPLER. And then, what I think is particularly important, section 4 of the bill provides that the Secretary of Agriculture and the Director of the National Institutes of Health shall annually review the research program conducted under this act in order to coordinate the program with the National Cancer Institute research program.

So, we are concerned primarily about two things. No. 1 is basic research on the diseases of animals, poultry, and wildlife. We are concerned about the economic factors concerned here in the diseases of animals and economic losses to livestock and poultry producers as well as ultimately the consumer who would buy that in the form of edible product.

Also, we are extremely interested in any corollary benefit that would come on the search for the causes of cancer. So we see this, really, a two-pronged attack, one that will result in some economic benefit to the livestock sector of agriculture as well as trying to find answers to questions on the causes of cancer and malignancies.

So, on the basis of the fact that this would not detract from the effort of the National Cancer Institute, could you support this bill if it were well coordinated with you and administered by the Department of Agriculture?

Dr. DEVITA. We certainly would support the intent of the bill as you state it, Mr. Wampler. I would point out that we do have a committee that has been in existence for 17 years whose main mission is to coordinate the efforts of a variety of Federal agencies, and the Department of Agriculture was one of the original members of that particular committee.

We do other things with the Department of Agriculture coordinated through that committee like search the world for plants to find drugs that might be useful for treatment of cancer.

Again, I believe the effort the Cancer Institute has put into it and has funds to put into the area of research in animals—and bovine leukemia is a classic example of how we benefit each other because the information generated on bovine leukemia has had worldwide implications that will ultimately, I think, lead to control of the disease in cattle.

There is a very fascinating side of bovine leukemia. There is no question that bovine leukemia is a virally induced illness. We do not have an example of that sort of thing happening in humans, so something went wrong somewhere along the line in the development of the virus that can cause cancer in cows. We have no assurance that this sort of thing will not happen in the future with humans, so we are very interested in studying bovine leukemia and continue to do so. I think it is a classic example of how the interests of the dairy cattle industry can overlap with humans in terms of cancer; we can save economic losses in herds, and we can find something about what we need to know about human leukemia and the relationship to viruses.

Mr. WAMPLER. The common complaint that I have heard from talking to a number of people that are concerned primarily with the research into the diseases of animals is that the panels who review all of the applications for grants for research funds so frequently do not have serving on those panels individuals with a discipline in veterinary medicine; usually it is other disciplines, and perhaps that is understandable.

Clearly animals can provide models which would be ideal, not only for finding the diseases in the animals, but also in human beings and correlating those data. So, the important thing here, I think, is that this would be an additional thrust into this vital area

research and one that, hopefully, would be coordinated so we ould minimize any possibility of duplication or overlapping. On at basis, then, you have no objection to the enactment of this bill. that correct?

Dr. DeVita. As you phrase it, yes, Mr. Wampler.

Mr. Wampler. Thank you very much. I appreciate your response.

Mr. de la Garza. Mr. Glickman?

Mr. Glickman. Thank you for your testimony.

I would just like to follow up a little bit on what Mr. Wampler id. Is it correct to say that although your statement indicates, d it may not be totally true, that most of the work you have ne on animal cancers is focused on their relationship with man cancers?

Dr. DeVita. The early work I cited in bovine leukemia was an empt to see whether viral induced cancers in animals would be usatively related to leukemias in humans, for example. If cattle rkers had a higher incidence of leukemia, it might be that there s transmission across species lines. So that was one way of king at it.

The other, of course, is to look at mechanisms. Reference was de to Marek's disease, which is a viral induced cancer in chick-. There is no other disease like it that we can really find. The us is easily identified—expressed. You can make a vaccine and cinate chickens. We are quite interested in why you have that ation in chickens and you do not have it in humans. We think breeding, of course, makes a huge difference in interpretation.

Mr. Glickman. Do you have a line item in your budget that is geted towards how much you spend on research into animal cers?

Dr. DeVita. No, sir, we do not.

Mr. Glickman. Is there any way you can estimate that?

Dr. DeVita. At the moment, if you look just at research in estic animals, we are spending $18.7 million a year, but it is a line item in the budget.

Mr. Glickman. How does that relate with previous years?

Dr. DeVita. That has been dropping somewhat. We have not put nany funds into the bovine leukemia research as we have in the t. The initial efforts require that we have large herds of animals he University of Pennsylvania and facilities for isolating large ds of animals. Once the work on the transmission was worked and once it was found not to be a public health hazard, the k shifted toward developing methodologies for diagnostic tests, ch is less expensive.

Mr. Glickman. Besides the bovine leukemia work, how has the ding been for other projects? Has it also fallen in terms of total e?

Dr. DeVita. Yes, because the standard nomenclature studies that us $1.5 million are essentially not requiring any more funds. have, in fact, terminated some contracts that have to do with loguing tumors in various species because of financial con-ints that have been placed on us. Yes, it has diminished ewhat.

owever, we do not look at it as saying, "Let's diminish our ort of domestic animal research." We blend the domestic

animal research with all other research so that when scientists discover a new virus in an animal system, they run to it and study it until they feel they cannot provide any more information from that system; then they move to the next system. So there is not any limit on funding for animal-related research.

Mr. GLICKMAN. The advantage to this bill is that it would provide for basic research into animal cancer for its own use, which may have spinoffs into human cancer. You might be still continuing the other aspect of it—the relationship to human cancer—and if there is appropriate coordination, we may actually move ourselves further along than we would have otherwise.

I think the work you do is probably the most significant work of any agency of the Federal Government. There are enormous benefits from the work of the National Cancer Institute. I just think that this is something where the veterinary side of the picture may be getting a bit short-changed on.

Let me ask you this. If an animal cancer grant comes to you—out of this 40 percent that you have accepted or some that you did not accept, were there some animal cancer grant applications that you did not accept?

Dr. DEVITA. I am sure there are. There are more grants that are actually approved by the study sections—the review bodies—than we can fund. And although I have not checked, I am sure there must be grants in there that are related to animal research.

Mr. GLICKMAN. I thank you for your testimony. I think you have pointed up some need for what I call separate, independent research on animal cancer which may not have a direct correlation with human cancer but spinoffs may exist. But, as Mr. Wampler said, I think this bill may be useful.

Dr. DEVITA. The only problem I see is being careful that the separation is not too wide. In fact, I think the history I recounted on bovine leukemia is a very good one because it tells you the people who were doing the very sophisticated research in human cancer stayed very close to the people who were doing the research in bovine leukemia. The ultimate effect was exactly the way you would like it to be, and we both gained from it. So, it can be too widely separated; cancer research is cancer research, and I would be a little bit concerned about that and about any kind of earmarking which always makes us very nervous in times of tight budget, as you mentioned.

Mr. GLICKMAN. I agree. Thank you for your testimony.

Mr. DE LA GARZA. Doctor, that is exactly what we hope that we can do. Since you use the animal as a carrier or to induce cancer in experiments, we hope that goes beyond the mice, that that information can be coordinated or made available to the animal researchers so it can work both ways: in working on the human cancer using the animal as the carrier, that information from that can be given to the sector which involves itself with the animal cancer.

Your fame has preceded you here, Doctor. I have had requests from several members to inquire about certain items within your jurisdiction. I apologize for doing so because it is really unrelated to our hearing, but to accommodate my colleagues, if you do not mind, but you are perfectly free to answer for the record or decline

if you so see fit. But I assured my colleagues that I would at least present you with the questions, both of which have been touched upon by you in your testimony, so I guess that would relate in some respects.

Dr. DEVITA. I would be happy to try to answer your questions.

Mr. DE LA GARZA. One is from the Subcommittee on Tobacco. They have asked me to ask you about the contract between the National Cancer Institute and Borriston Labs. Are you acquainted with the use of dogs for inhalation of smoke?

Dr. DEVITA. Yes, I am, Mr. Chairman.

Mr. DE LA GARZA. You are acquainted with that?

Dr. DEVITA. Yes, I am familiar with the contract. We terminated the contract.

Mr. DE LA GARZA. What can you tell us about that, or what was the reason for terminating it, or what was the end result or finding?

Dr. DEVITA. Well, there is no end result at the moment because the contract is in the process of being terminated, but we had two large studies that were examining the toxicity of various tobacco products by using dogs to inhale the cigarette smoke. This particular one was primarily looking at the toxicity of nicotine. We felt that we would rather redirect our efforts in the smoking and health program to finding ways to explain to young people—teenagers and so forth—and have them understand why they smoke so we could try to get into smoking cessation in a bigger way, and not to do research which might be viewed as to develop a less harmful cigarette. Given the limitation on our resources, we had to make some priority decisions, so we terminated one of the contracts; that was the Borriston contract.

It was to go for a few more years. But we terminated it by asking them to sacrifice the animals at this point in time and do the studies that they were going to do at this point in time rather than a couple of years from now. That is what we did.

There has been some question as to what the implications of this are. One of the questions given to me on numerous occasions is, "Are we throwing away our investment in this?" The answer is that we are not; we are going to examine the animals at this point in time.

Mr. DE LA GARZA. How long did the research continue?

Dr. DEVITA. I think it was only a couple of years, Mr. Chairman; I do not know the exact duration.

Mr. DE LA GARZA. To your knowledge, was there any scientific evidence obtained that the dogs suffered any adverse medical effects?

Dr. DEVITA. I know none of the data yet; they have not been analyzed. But they will not be discarded. It was not done because of a conclusion that we developed in a study that we might not like. This has been implied by some people. It was done strictly for economic reasons. There was a shift in emphasis of the program to prevention of smoking from developing a less harmful product, more in the purview of the companies that manufacture the product.

Mr. DE LA GARZA. Also, some of our colleagues have inquired as follows. You mentioned the cancer eye. We have had some inquir-

ies concerning that. I was reading your statement and listening to you on how important this program was and how successful, but some of my colleagues tell me that you terminated the contract.

Dr. DEVITA. The contract to support this, which was a much larger contract, is being phased out—yes. One of the reasons for that, Mr. Chairman, is that we move from field to field depending on what we are learning and what we want to do to apply that particular knowledge.

One of the early interests in cancer eye, when we were beginning to examine BCG, which is the tuberculosis vaccine, about 10 years ago, was whether, in fact, BCG would have any kind of effectiveness in controlling cancer. We now know both where it can do it, and that is the local injection into tumors—and this was a model for that—and what it cannot do, which is, when given as a systemic, that is, injected under the skin to control cancers of a more widespread type, it has essentially no effect.

So we have moved on to other things and are applying this knowledge. In the dairy cattle industry, there is a way of controlling the tumor locally. In humans, in the few circumstances where BCG can actually be given on or in the tumor—skin cancer I mentioned but also in localized bladder cancer—we are applying the knowledge. Again, with limited resources one has to set the priorities as to what one does tomorrow so that we continue to move ahead. That is the only reason for us shifting our emphasis away from supporting the routine model that we have set up with the cancer eye program. We did this with the advice of a lot of individuals who came to look at the project.

Mr. DE LA GARZA. I understand that one of these contracts was with a Dr. Kleinshuster of Utah State University.

Dr. DEVITA. That is correct.

Mr. DE LA GARZA. And that contract has been terminated?

Dr. DEVITA. I believe that contract is being terminated—yes.

Mr. DE LA GARZA. And your information to us, for transmittal to my colleagues, is that it was purely for economic reasons?

Dr. DEVITA. No, not purely. It was in rank order of scientific priorities. We feel we have learned a lot from that system and can learn a lot from other things, so we have redirected the money.

I believe that what I cited in my testimony is a correct representation of the value of that model for the dairy industry and for us. It is just that we do not wish to spend all our time injecting BCG into the model. We would rather go on now and study different things.

Mr. DE LA GARZA. This is one of the areas unrelated to the questions—from my colleagues—where it looks like the thrust of the bill that we are holding hearings on and the work which has been done really relate, one to the other. I was happy to see you make mention of that in your testimony.

I do not know fully the extent of the termination of the contract, and the work, and what more can be done, but I would very respectfully suggest that if it is at all possible, because that is exactly what this subcommittee is looking for, we offer you, to the extent that we have any jurisdiction, any assistance that we can.

We are looking forward to some joint hearings with the Science Committee and the Health Committee which have the basic juris-

diction—either one or the other or all three committees having joint hearings—in order that we might at least coordinate the information which we get here in the Congress and relate it to our basic jurisdiction which is the agricultural sector.

Dr. DEVITA. May I comment on that reduction again, Mr. Chairman, because I do not want to create the impression that we are reducing our support of research in domestic animals proportionately greater than in other areas?

In the past 6 months, the staff at the National Cancer Institute and I went through 1,500 of our contracts, one by one, in order to make some economies and redirect funds and were able to recoup a substantial number of funds. These contracts you mentioned are two of them, and they are a very small fraction of the reductions that we actually took on all the contracts.

It is just that when you do this sort of process it has an effect throughout the program. So we have not disproportionately aimed our reduced effort at the animal research. We still, I feel, are enthusiastic about the research we do with domestic animals, and I tried to convey that in my testimony.

Mr. DE LA GARZA. We thank you for that, and, again, we beg your indulgence in answering the other questions that were submitted by our colleagues.

We appreciate very much your being here and look forward to a continued association with you.

Dr. DEVITA. Thank you for inviting me.

Mr. DE LA GARZA. We have a vote on the floor of the House which I think is a recorded vote.

Do we have a problem timewise with Dr. Rauscher or Dr. White? Dr. Rauscher, do you have a problem with time?

Dr. RAUSCHER. Not really, Mr. Chairman.

Mr. DE LA GARZA. Dr. White, you do?

Dr. WHITE. My problem will come up at approximately 12 o'clock.

Mr. DE LA GARZA. I think we will be finished long before that. So, let us take about a 10-minute break to allow us to make our vote. The subcommittee will stand in recess.

[Recess taken.]

Mr. DE LA GARZA. The subcommittee will be in order.

We will invite Dr. Rauscher and Dr. White. Would both of you come to the witness table? We are anticipating another vote, so, without objection, both of your statements will appear in the record as if given. If you would care to summarize, it would be helpful.

STATEMENT OF FRANK J. RAUSCHER, JR., PH. D., SENIOR VICE PRESIDENT FOR RESEARCH, AMERICAN CANCER SOCIETY, INC.

Dr. RAUSCHER. Thank you, Mr. Chairman. May I say that it is a pleasure and privilege to be back with you again.

In fact, I was going to ask you for permission to insert this in the record so as to save you some time and inasmuch, also, as some of the material has been covered, at least in part, by former witnesses.

Mr. DE LA GARZA. Thank you. Without objection, it will be inserted in the record at the conclusion of the testimony.

Dr. RAUSCHER. May I say at the outset that the American Cancer Society and I, as an individual, strongly support this bill. I think it is very apparent that you are filling a void, which is very critical with something as important as cancer. You are trying to cover things that cannot readily be covered any more by the National Cancer Institute or, for that matter, by the voluntary sector. So, I think we would all agree that what you are trying to do is terribly important, and timely.

In looking over the testimony of former witnesses, I note that there were a number of questions that seemed to be important to this committee, and let me just comment on those.

The first is, what has been done in recent years to find out whether some cancers in humans and animals are definitely linked to viruses. Suffice it to say that since 1972 at the outset of the expanded national cancer program, well over $1 billion has been provided, by the Federal Government largely, but also by the private sector, in part for studies in viruses and cancer. I think that is one thing that attests to the importance that the scientific community would ascribe to this—and the Congress, I should say, would ascribe to this area.

Second, it seems a central theme has been, what do we know about the public health dangers in virus infected animals? That is, are animals or their causative agents, such as viruses, transmissable to people?

I would agree with Dr. DeVita and Dr. Potter this morning, and others, who say there is no evidence that this does occur in nature. On the other hand, inasmuch as we know of well over 100 different viruses capable of causing cancer in virtually every animal phyla known to us, this does not mean that we should not be very wary of the possibility that some time in the future such a relationship might be discovered. Hence, all the more important is the work that this bill may be able to fund in the near future.

If I may, as I was asked to yesterday, I would spend a few minutes bringing the subcommittee up to date on the viral aspects of human cancer and, in particular, what we are planning to do in terms of prevention.

I might add also that much of what we are capable of doing today has come directly out of studying viruses in animal systems and their induced cancers.

In terms of cancer prevention today, we do have enough information at the present time to prevent about 60 percent of the many diseases we call cancer. Unfortunately, much of this has to do with paying attention to our bad habits or picking up better habits. Consequently, one of the major approaches to cancer prevention is in the whole area of behavior modification. How do you get people to give up those things that are not good for them? Not much work has been done on this, unfortunately, but much more will be in the coming decade of the 1980's. Giving up smoking is just one example of how we can better our lives through better habits.

The second major approach, of course, is to clean up the environment. This is something we talk about all the time but is exceedingly difficult. Nonetheless, this will proceed. Cleaning up the

environment also means providing a better environment for our domestic and wild animals. It may also mean someday eradicating those diseases in animals that may put man at high risk.

As you may remember in the early 1960's this is exactly what was done in one of the foremost dairy nations of the world where the Danes killed off up to 30 percent of their cattle because they carried what appeared to be a lymphocytosis, that is, a high count of white cells in the peripheral blood. That took a lot of courage, but, at the same time, they were convinced that this would save the dairy industry in Denmark, and so it has, apparently.

One other approach that you are going to be hearing a great deal more about in the decade of the 1980's is a whole new area called chemoprevention. That simply means, are there materials, such as vitamins, perhaps, at high doses, or materials such as interferon, which may very well be a prototype of a whole new class of biologic response modifiers, as they are being called now, that may not only be useful in therapy of existing cancer but in the prevention of cancer in those people at high risk?

Already we have several trials underway in this country to try to prevent early bladder lesions in workers exposed to aniline dyes from developing into full-blown cancers. I have no doubt that other trials will begin very soon with additional compounds.

Finally, in terms of what is new in trying to prevent cancer, there are vaccines. This is something we have been dreaming of for many years. But now, with a lot of work coming out of studying the virology of animal cancer, we are able to apply that technology to human viruses which are highly suspect as causing cancer in people. There are four of these: Herpes simplex viruses I and II are those that are known to be able to induce, if you will, transformation or cancer in human cells grown in the test tube. It is thought by many that herpes simplex type II, in particular, may very well induce cervical carcinoma, penile carcinoma, and others, in people. Vaccines are under development there.

So too would a virus called EBV, another herpes virus that induces infectious mononucleosis in people and possibly several forms of cancer. It is likely that within a year or two trials will begin with material made from that particular virus.

There is a fascinating trial underway right now, and within 2 weeks the results of the first tests will be announced. That is, people have been able to develop a vaccine against hepatitis B virus, isolated just a few short years ago. The hope here is that that vaccine will prevent active disease in more than 30 million people in the world who carry that virus right now or who have active disease.

People infected with this virus are highly predisposed to hepatoma, a primary tumor of the liver. So it is hoped that by preventing hepatitis B carrier states or active hepatitis we will also prevent tumors of the liver, which is a very serious problem in many parts of the world.

Again, I am giving you just a few examples—there are many others—of technology coming out of studies with animal viruses in domestic or laboratory animals that are already making an impact, or a potential impact at least, on our being able to better control cancer in people.

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May I close by congratulating you again for coming to grips with a very important problem; for filling a void. I said before, these are studies which must continue. Without your support, it may very well be a large block of studies that would fall through the cracks.

Again, Mr. Chairman, I am pleased to be with you and I support this bill.

Mr. DE LA GARZA. Thank you very much, Doctor. If you would stand by while we hear from Dr. White, we may have a couple of questions.

[The prepared statement of Dr. Rauscher may be found at the conclusion of the testimony.]

STATEMENT OF DR. JACK E. WHITE, DIRECTOR, CANCER CENTER, COLLEGE OF MEDICINE, HOWARD UNIVERSITY, WASHINGTON, D.C.

Dr. WHITE. Mr. Chairman and members of the subcommittee, it is a pleasure to be here. I am very pleased and grateful to you for having invited me.

Mr. DE LA GARZA. Thank you, Doctor. Without objection, we will insert your full statement.

[The prepared statement of Dr. White may be found at the conclusion of the testimony.]

Dr. WHITE. One of the advantages of being last as a witness is that most of the sensible and useful testimony will have been given to the subcommittee.

I think that studies of cancers in animal populations—spontaneous cancers—may well shed some significant information that may be utilized in understanding human cancer. Beyond that, there is an economic and also an important agricultural reason why we would like to see this research in animals continue, one being producing safe and better animal products for human consumption.

The investigators at Howard University have done considerable epidemiological research which shows an ever increasing incidence of cancer in humans, especially among men and particularly black men. The mortality rate is considerably higher in the black male population than it is in any of the other sex or racial groups. We do not know the reason for it; we suspect that it has to do with environmental influences including poorer socioeconomic status, poorer general health; so survival is poor—survival at every stage of cancer, whether early or late. It is worse in black people than it is for people in the general population, and we believe that this is due to a high incidence of associated diseases as well as generally poor health. The incidence accounts for only about 30 percent survival; this accounts for about 70 percent of the differences between the races.

I might say that our epidemiology program at Howard Cancer Center is being led by an epidemiologist who happens to be a veterinarian as well. That is an interesting kind of interchange that allows for us to have some overlap between animal types of consideration and human, especially from the epidemiologic standpoint.

We are also looking into some basic aspects of the cancer problem there. But before going into that, I would like to state that Dr. Potter has already talked about some of the interactive programs

between the Howard Cancer Center and the Georgetown Cancer Center—the infraoperative therapy. We are impressed with its utilization for certain types of cancer. What it does, basically, is allow us to get in a larger dose of therapy in certain specific situations that would be limited. We are able to get in more radiation therapy that way without damaging normal tissues.

We are studying, in our basic science area, largely cell membrane alterations in cancer and comparing that, trying to make some interpretation of what is taking place between malignant and normal cells.

We have also started a biochemical program, looking into the biochemical nature of the antiviral activity of interferon. That is a fascinating program.

My only concern about this bill is whether or not it will have a significant impact on the National Cancer Institute's program and whether there will be fragmentation of efforts. It seems to me that the strongest contribution this bill has will be to continue the basic epidemiologic research in this area and then put that to laboratory tests afterwards. But I do have concerns about fragmenting the already existing cancer programs.

With that, Mr. Chairman, I would like to terminate this portion of my testimony and answer the questions which you may have.

Mr. DE LA GARZA. Thank you very much, Doctor.

We appreciate your being here—both of you. Your testimony, of course, will be very helpful as we proceed with this legislation.

Mr. Wampler?

Mr. WAMPLER. Thank you, Mr. Chairman.

I have no particular questions, other than to thank Dr. Rauscher and Dr. White for coming this morning and testifying.

Let me say to you particularly, Dr. White, I earlier shared some of the same concerns that you expressed about this bill. If it were in any way to result in fragmentation of our basic thrust into cancer research, I would be opposing it because I have been and hope to continue to be a strong supporter of our basic research into causes of cancer and the treatment and cure of cancer.

But as I envision this bill, it will be supplemental to it. What we are stressing here—and the bill is very specific—is that there be total coordination with the National Cancer Institute and the Department of Agriculture to be sure, to the maximum degree possible, that there is not duplication of effort or overlapping of effort.

Earlier witnesses testified—particularly Dr. Marshak who is the dean of the School of Veterinary Medicine, University of Pennsylvania—as to their deep concern that there was not adequate funding for research into cancer in animals and pointing out the great work they have done in the herd that they have there in their facility, which I think most people concede is a model herd for certain tests.

So, I share your concern about it. I think the bill is rather specific in that regard. But as the bill moves through the legislative process, let me assure you and others, it will be my purpose to make it just as clear as we possibly can that there is not to be duplication of effort, that to the maximum degree possible we will provide the safeguards that will prevent that type of thing; and,

secondly, if this is an authorization bill, that we follow through to be sure we get an appropriation to carry out the intent of it.

So, I share your concern, and I appreciate your bringing it to the attention of the subcommittee. I only wish it were possible for us to appropriate even more money because, as was pointed out earlier by Dr. DeVita, only 40 percent, I believe, of the applications that they now have at the National Cancer Institute, is being funded. I do not envy them their task of trying to put some degree of priority on which ones will be funded and which will not. We see a real possibility here of a significant contribution into the basic research of the causes of cancer in humans as we try to find these in animals, poultry, and wildlife.

I just want you to know that you raise a very valid concern but one that we are not unmindful of. I want to assure you, to the degree that I can, we will see that that does not happen.

Dr. WHITE. Thank you, Mr. Wampler.

Mr. DE LA GARZA. I would like to do the same. I echo the words of Mr. Wampler, Dr. White.

Walking to the Capitol, Mr. Wampler and I were discussing that we did not find any veterinarians working in the human side of cancer, and I am happy to hear that you do have one on your staff.

Let me ask this of Dr. Rauscher. I must admit that I am learning a new vocabulary; this area is altogether out of my field. Why is it—if there is an answer—that the bulk of the research is done on mice or rodents?

Dr. RAUSCHER. I think there are several reasons, Mr. Chairman. One is that it is simply historic. Some of the first tumors were found in mice. Many of the studies that have led into what we are doing today derived exactly from that.

No. 2, they are far less expensive.

No. 3, you do not need barns to keep thousands of mice available.

And, probably as important as anything else, you can inbreed them so that you can run valid, reproducible experiments. This has not been possible in larger, domestic animals.

Mr. DE LA GARZA. I suspected some of that. But in the testimony of the doctor from the Smithsonian Insitution that catalogs, we could see the variety of all the animals—fish, fowl, et cetera.

Dr. RAUSCHER. Yes. That is a major contribution to our understanding of the cancer process—absolutely.

Mr. DE LA GARZA. In the areas such as space travel, et cetera, they take the closest to the human, which is the monkey. But I guess the quartering availability and so on would have a bearing on it.

Dr. RAUSCHER. Yes. With primates especially it is a problem. India no longer allows exportation. That is a holy kind of animal in many parts of the world, and it takes a long time to set up breeding colonies in this country, and it is terribly expensive. The problem there is that when you use monkeys you are apt to have to wait 25 years or more before you terminate an experiment, whereas with a mouse it is usually 1 to 2 years.

Mr. WAMPLER. Would you yield on that?

Mr. DE LA GARZA. Yes, certainly.

Mr. WAMPLER. What is the experience with a model dairy herd, for example?

Dr. RAUSCHER. The BF1 herd is something that NCI began supporting in 1964, as I recall. That is a most unusual herd because there are clear lineage records on each of the animals. Therefore, one can determine whether that virus which causes the leukemia, or lymphosarcoma, is transmitted not only horizontally—that is, you sneeze at me, and I sneeze at you—but whether it is transmitted through the germ cells—vertically. That is terribly important. You can do that in animals, and so far as I know, Bob Marshak is the only fellow who has done it in a domestic animal of that size.

Mr. WAMPLER. Of course, Dr. Marshak was before the subcommittee earlier and made an excellent contribution to these hearings. I am vitally interested in the work that is going on in that one facility.

Dr. RAUSCHER. So am I.

Mr. WAMPLER. We certainly would envision that, under the terms of this legislation, that would be one of the high priority projects.

Dr. RAUSCHER. I would certainly hope so.

Mr. WAMPLER. Thank you.

Mr. DE LA GARZA. We thank both of you gentlemen.

Dr. Rauscher, looking at your curriculum, your honors, and recognitions, speaking from the political side, it looks to me like you ought to run for something.

Dr. RAUSCHER. I will leave that to you gentlemen. Thank you.

Mr. DE LA GARZA. Thank you very much. The subcommittee will stand adjourned.

[Whereupon, at 11:50 a.m., the hearing was adjourned.]

[Prepared statements submitted by witnesses and additional material submitted follow:]

STATEMENT OF DR. VINCENT T. DeVITA, DIRECTOR, NATIONAL CANCER INSTITUTE

Mr. Chairman and Members of the Committee:

I am pleased to have this opportunity to discuss the National Cancer Institute and our program of research on the causes and treatment of human cancer.

The NCI was created by an act of Congress in August of 1937. We were, in fact, the first of the 11 research institutes that now constitute the National Institutes of Health. In 1937, our budget was tiny and our assignment enormous. We were charged with serving as the principal research agency of the Federal Government, on behalf of the American public, for investigating scientific solutions to the problem of cancer. We have grown rapidly since then. The National Cancer Act of 1971 and the Amendments of 1974 and 1978 increased by four-fold the level of support for cancer research and gave us additional authority to plan and develop the National Cancer Program. This program has emerged as a coordinated, international cancer research effort. It includes centers located around the United States for research, training, and the demonstration of advanced methods for controlling cancer. Fully one-third of our budget goes to research on cause and prevention. Another third funds our program that supports basic research in treatment and the development of anticancer drugs. The balance funds research in detection and diagnosis and our community based demonstration projects.

Over 47 percent of our funds are used to support research grants. Ideas for this research are submitted to us by investigators at universities and other private institutions around the country. Funding of grant applications is determined primarily from advice of peer review committees of other scientists working in the same field as the grant applicant. NCI grants currently support 3000 investigator-initiated research projects.

Expansion of the NCI in 1971 not only provided more funds for cancer research but also gave the NCI increased freedom and flexibility to operate its programs. Mr. Chairman, we have made notable progress. The cancer mortality rate for Americans under the age of 55, for whom cancer continues to be the major cause of death from disease, is decreasing. Fully 41 percent of patients with cancer now can expect to be cured with

currently-available treatment, compared to 33 percent in 1955.

I would like now to address the concers of the Committee on cancer research in domestic animals. Although the mission of the NCI is to find ways to reduce the cancer burden for humans, animals have served the scientist well as models for many human diseases, and in serving this role, animals often benefit from research findings.

I would like to cite some examples where animals have given us important information about cancer in man and where we have in turn been able to provide information that would reduce cancer among domestic animals.

In 1964, with a special $10 million appropriation from the Congress, the NCI began an intensified research program on cancer viruses. One of the program's four targeted research areas was to explore the nature of animal leukemias and their relationship to humans. Our concern was to determine whether animal viruses posed a human health problem. Two important findings came out of this endeavor. One concerned the relationship between leukemia in cats and that in humans. In 1965, virologists isolated a cat leukemia virus that caused cancer in a variety of animals, including dogs, cats and monkeys. The virus could infect human cells grown in culture. NCI conducted a large study in California in the late 1960's that surveyed cat owners and veterinarians to determine whether they were at higher risk to leukemia than the general population. This study could find no evidence that the virus could cause human leukemia nor that cat owners or handlers had an increased risk of leukemia.

We continue to study cat populations to learn more about how the viruses that are endemic in these animals sometimes are expressed as cancer. One of the potential benefits for veterinary medicine is the development of a vaccine to prevent cancer among this population of domestic animals.

The second finding contributed by the Virus Cancer Program concerns leukemia in dairy cattle. Evidence available in the 1960's suggested that leukemia in cows might be caused by virus particles present in the milk. Studies done by Virus Cancer Program scientists suggested that the usual pasteurization methods inactivate animal viruses present in cow's milk. We could assure the general public that children and adults are not at risk to developing leukemia from consuming milk and milk products that have been pasteurized. In addition, NCI has surveyed blood samples

from thousands of cattle handlers. We were looking for antibodies to the bovine leukemia virus. The presence of such antibodies would be evidence that a person had been exposed to the virus. Mr. Chairman, I can report that no evidence of antibodies to bovine leukemia virus were found in human serum. While bovine leukemia virus continues to be a serious economic problem for farmers, it does not appear to be a human health problem.

We continue to study leukemia virus in cattle herds. Our studies indicate that in some herds over 20 percent of cattle have antibodies to the virus. Of course, the incidence of clinical disease is much lower.

NCI-supported scientists have developed sensitive probes to look for footprints of the cow leukemia virus in other species to learn more about how the virus is transmitted. They have found that bovine leukemia virus infection is much more prevalent during the summer months, and they have isolated virus from horseflies that feed on infected cattle. We now think that this insect helps transmit the virus from one cow to another. Another recent finding is that infected cattle have a factor in their blood that inhibits leukemia virus expression. This may help explain why many cows seem to carry the virus, yet few show signs of the disease.

The Virus Cancer Program turned up no positive and considerable negative evidence that cancer in man is an infectious disease. We had cast a wide net to search for an animal cancer virus that posed a threat to humans and none was found. Cancer causation is complex, and viruses are probably better considered in terms of risk factors rather than as "cause" in the strict sense. A risk factor increases the chance that a person would get cancer from other agents, and provides an opportunity for prevention.

By 1970 much evidence was converging to suggest that the environment including lifestyle played a determining role in cancer causation. This observation implies that cancer can be prevented, or its incidence greatly reduced, by identifying those factors and trying to reduce or eliminate exposure to them.

One of the programs that falls under the pervue of our prevention efforts searches for clues to environmental cancers using domestic animals as sentinels. This program actually began in the mid-1960's. At that time the veterinary profession had no standardized way of classifying animal diseases. NCI cooperated with veterinarians to develop a standardized

nomenclature of all diseases in domestic animals. The system was computerized and adopted by the majority of U.S. veterinary school hospitals by the mid-1970's. Over 41,000 animals were found to have tumors. This data base now provides us with descriptive information on trends of cancer in animals breathing the same air and drinking the same water as humans.

Using this source, NCI epidemiologists recently found that bladder cancer among dogs was highest in areas with alot of industrial activity. We had seen a similar pattern for human cancer in our county-by-county survey of cancer mortality.

Finally, I would like to just briefly mention the work of the NCI on bovine "cancer eye". This is a squamous cell carcinoma that poses a problem especially for dairy cattle. NCI immunologists became interested in cancer eye because they were looking for an animal model that might help us design better ways of using immunotherapy to treat human cancer. Cancer of the eye in cattle was of special scientific interest because unlike rodent cancers it occurs naturally in an outbred population of animals. More importantly, the cancer metastasizes to the lymph nodes in a way similar to human cancer. One of the first experiments done in the bovine system was to test new methods of administering a tuberculosis vaccine, BCG (bacillus Calmette-Guerin). This strain of bacteria was being studied extensively in attempts to stimulate the body's immune system to reject the growing cancer.

Injections of a BCG preparation directly into the eye tumor cured a substantial number of cattle, and the treatment continues to be of value to the cattle industry.

We have taken the lessons learned from this study and are currently using intratumoral injections of BCG to treat cancer patients with melanoma. Like cow eye, this human skin cancer is thought to be caused by excessive exposure to sunlight.

These are only a few examples of all that we have learned. Often we accomplish two purposes. By trying to learn more about human cancer, we also learn more about cancer in animals. Though we do not fully understand the causes of cancer, I would be very surprised that we find a major difference in the mechanism of these diseases between man and his companion animals.

Mr. Chairman, this concludes my testimony. I shall be happy to answer questions.

Testimony of

Frank J. Rauscher, Jr., Ph.D.
Senior Vice-President for Research
AMERICAN CANCER SOCIETY, INC.

Mr. Chairman, I appreciate the opportunity to appear before this Committee and to address its interest in cancer virology.

The American Cancer Society's review of your prior hearing testimony has identified four questions which several of the Committee Members might share and I shall give brief answers to these questions:

1. First, what has been done in recent years to find out whether some cancers in humans, as in animals, are definitely linked to virus infections?

The answer is that the National Cancer Institute has awarded contracts to mobilize scientific interest in this vital question, has organized seminars, study sections, held conferences to set priorities, has awarded support contracts for reagents and other laboratory materials and instruments so that government and nongovernment researchers could move ahead with dispatch. They have moved ahead in force. No longer is it necessary to urge them forward with contracts. Both the American Cancer Society and the National Cancer Institute viral oncology research programs now work practically all the way with investigator-initiated, regular research grants that are peer reviewed for quality and relevance.

2. What is the scope of this work? One might say that it represents the world's largest organized effort in biology. Hear are the figures:

1972	$48.2 million	1977	$100.2 million
1973	64.5 "	1978	108.7 "
1974	71.7 "	1979	110.4 "
1975	92.9 "	1980	104.8 "
1976	102.0 "		

3. What do we know about the public health dangers lurking in virus infected animals? Mr. Chairman, I agree with your veterinary and human medicine witnesses who state that the preponderant weight of scientific evidence is that human cancer is not an infectious disease. I

also agree that, in the absence of scientific proof of how cancer develops in humans, it is important to devote some portion of the nation's cancer research effort to further investigation of the action of viruses in human and animal carcinogenesis. Therefore, I support S. 2043, the Animal Cancer Research Act.

4. Last, I think the Committee asks, "what more needs to be done?" The mandates of the National Cancer Institute and of the private organizations working on cancer stop where the direct link with the human conditions stops. My experience with the House and Senate Appropriations Committees tells me that the National Cancer Institute might be duly criticized if it went beyond that mandate. Therefore, I sincerely commend your Subcommittee, Mr. Chairman, in pursuing S. 2043, because there is no question that potential economic losses in terms of condemned dairy herds, loss of beef and other exports, reduced milk and meat productivity resulting from viral infection, and the significantly reduced, but continuing, losses in the poultry industry, all warrant intense research, long overdue research, which is within the province of the Department of Agriculture. There are present losses. Without effective research they will become worse.

As your bill wisely recognizes, there are common human health interests to be pursued in this research. Coordination between USDA and NCI is essential and deserves your continuing oversight, once this legislation is enacted.

Those are the brief answers. If I may, the rest of this testimony will be my way of adding details for your consideration.

If, Mr. Chairman, Members have additional questions, my career-long interest in virology is at your disposal. I think scientists are obligated to explain their work in terms laymen can understand and I am willing to try to answer any of your questions.

Going back to the first question, What's been done in this area of research? The cancer research community's interest in this area

was described by a National Panel of Consultants appointed by the United States Senate. The Panel told the Congress (Senate Document 92-9, 92nd Congress, First Session) in April of 1971 that, "Some one hundred viruses now have been discovered which cause cancer in some species of amphibians, birds, and mammals. Although there is, as yet, no unequivocal evidence of a human cancer virus, most investigators working in this field are of the opinion that viruses will soon be shown to be responsible for some types of human cancer." We had some very specific leads. For instance, a virus called "EB virus" appeared in electron micorgraphs of cells of Burkitt's tumor, a disease afflicting children in Africa. All of the African children with Burkitt's tumor have significant amounts of antibody against this virus while less than half of other African children have such antibodies in their blood. We also knew at that time that a group of RNA-containing viruses had been seen in samples of human milk and in human breast cancer cells growing in tissue cultures. These viruses resembled the mouse mammary tumor virus which is transmitted from mother to offspring in genetically susceptible strains of mice. C-type viruses were then known to induce leukemias and sarcomas in cats, chickens, and mice and such viruses had been detected in specimens of human leukemias and lymphomas.

Because it was unethical to inject a suspected virus into humans to see if cancer occurred, our studies, as in many instances throughout medical history, turned to animals.

Even at that time we saw these viruses mainly in animals closely similar to each other genetically. In places where most human cancers are under study there are no such closely inbred human families. As you know we have developed laboratory and farm animals which are very highly inbred.

With these facts in mind we, therefore, invested heavily in virus and related research, starting with $48.2 million in fiscal 1972 and moving ahead according to the pattern in the table above.

To show you how big an emphasis the National Cancer Institute thought, years ago, and thinks today is the proper emphasis for virus studies, the year by year data could be put in percentage terms as well as raw dollars. In 1972 more than one dollar in every eight appropriated to the National Cancer Institute, 12.9%, was invested in viral oncology and related research. In 1976 the proportion was 13.4%. It has declined this year to an estimated 10.4%, but that is still a large share of the $1 billion National Cancer Institute budget.

You might be interested to know that in 1972 about $42 million of the $48 million in the Institute's virus work was channeled into contracts. The situation has been reversed as more and more researchers have seen the value and the potential of this work. This year less than a third of the virus work will be supported through contracts.

There has been some testimony on this bill and discussion by some supporters of it on the point of how much of the proposed authorized funds should be spent directly by the Department of Agriculture and how much by individuals and laboratories getting grants and contracts from the department. This year at the National Cancer Institute I am informed that both in-house research and the management of grants and contracts performed extramurally will take only 27% of the Institute's outlay for virus research. The rest, or 73%, goes to people outside of the government on the basis of peer review and contract terms mainly designed to provide assistance to the whole program, to produce reagents and other laboratory materials, to produce tissue cultures and perform routine testing, sometimes to preserve samples of various virus strains that will be called upon as research progresses. My judgment, based only on my NIH experience, is that the majority of actual research is best performed outside of government so long as the agency with grant and contract jurisdiction has enough funds to maintain a highly competent cadre of scientists to keep up with current developments to get a grip on questions of priorities, to keep up some research work of their own, and to give sophisticated mangement to the

extramural program. Science being what it is, my guess is that the 73%-27% split between inside and outside work at NCI is not far off what might be productive at USDA and you might want to mandate that in your legislation.

Mr. Chairman, from time to time people not directly taking part in cancer research wonder why there is not a human cancer vaccine. I think that we made great efforts in that area. For instance in Africa we established a team and helped build clinics and laboratories to study intensively the very rapidly growing Burkitt's tumor, which develops in a few weeks into head and neck tumors. Because it definitely involves a virus and because the effect of a vaccine could be shown quickly in this fast-acting type of cancer, we thought we had an excellent research approach. However, we found that carefully administered chemotherapy, at that time the only therapy of proven, if partial efficacy, was curing more and more of the patients. When the proportion rose near the 90% level as we learned better how to treat these patients, it became unethical to subject them to experimental treatment with a much lower initial chance of success. That effort took many resources. We had to send scientific and medical teams to another continent. We had to train care personnel. We had to build a system to bring in the patients. We had to engage in international negotiations to win the confidence of the government, the workers, and patients that we needed to perform the experiments.

There were other efforts just as large made at the same time. None of them over the years convinced either the participants in the program or the critics of the program that we knew enough to invent a human cancer vaccine, so basic studies have continued.

Mr. Chairman, I think that this Committee might want to be aware that the National Cancer Institute's virus program has often attracted severe criticism. Honest differences of expert opinion are involved. As you move ahead with your oversight and your legislation you might want to be familiar with the ongoing debate.

The Senate's National Panel of Consultants said (page 3 of their report), "There have been major advances in the fundamental knowledge of cancer in the past decade, and these advances in knowledge have opened up far more promising areas for intensive investigation than have ever heretofore existed. These areas of special promise must be explored with vigor, if we are to exploit the great oppotunities that lie before us." Then the Panel recommended, "Among the areas of special promise are: (a) The identification and study of the chemical, physical, and other environmental factors that cause cancer (food additives, air pollutants, industrial hazards, radiation, and other carcinogens);

"(b) Viruses causing cancer (what viruses cause cancer, how are they transmitted, and how do they act);" etc. So virology was near the top of their list of eleven areas of recommended concentration.

Nobel Prize Laureate James D. Watson said a few years earlier in Molecular Biology of the Gene, published by W.A. Benjamin, Inc., NY, 1965, "Many intelligent biochemists hold the view that now is not the time to work seriously on the biochemistry of cancerous cells. They argue that, even though cancer cells are the cause of enormous human suffering, nonetheless it does not make sense to put a disproportionate share of our scientific effort into trying to meet an unripe intellectual challenge. They compare the current situation with the desire to understand the nature of solar energy at the time of Newton." Then Dr. Watson, the co-discoverer of the double helix which opened a whole new area of biological research, said, "I suspect, however, that this pessimism may not be justified." Three years later he became the director of a laboratory devoted almost entirely to viral oncology research.

In 1973 the critics of the concentrated program recommended by the Panel of Consultants, enacted by the Congress, and administered by the National Cancer Institute, were instrumental in convincing me that, to make sure the broad scientific community knew how our decisions were made and to have confidence in them, that a special scientific investigating

committee should have access to all our records. The National Cancer Advisory Board authorized the committee.

After the committee made its report, the House Subcommittee on Labor/HEW appropriations devoted some of its hearings on National Cancer Institute funding to the findings of the critics. The Chairman asked me, "Do you think that the fundamental idea of the Special Virus Program, that is, gambling that a basic research idea, could be the one to constitute a scientific breakthrough, do you think the fundamental idea is wrong or a mis-use of money? Would you do it again?"

"This is one of the best ways to use funds for disease oriented research and I would certainly do it again." I mentioned that, "Many experiments took two to three years to complete in animal systems. One task, therefore, was to encourage people to apply for support through this program for studies that were deemed very promising and very important to the control of these cancers in people. The contract mechanism was used in order to get the program going more quickly. At that time, we were able to award contracts to academic or commercial investigators within about three to three-and-a-half months. It took about nine months to review and award a grant after the investigator wrote his application and submitted it to NCI."

I told the Appropriations Subcommittee that there were bona fide concerns expressed in the report on the virus program and that NCI had made administrative changes to meet these concerns and to let the whole scientific community know how we were operating.

One result of that investigation was a listing of what had been accomplished up to that time.

1. Maybe the greatest accomplishment of all is that we attracted large numbers of creative brains to the program. With 131 contracts, for instance, the Virus Cancer Program in fiscal 1973 supported 600 professional scientists of many disciplines. Further, associated with this work was the training of 230 scientists working just prior or just after ap-

ceiving their post-graduate degrees. In other words, we were catching them after most of their education was well along, or completed, and encouraging them to focus on this problem, this plague of cancer.

2. This focus was rewarded. In an early year of the program there were 1,183 publications of scientific findings.

3. RNA viruses: By 1975 the program had identified two major groups of oncogenic RNA viruses; learned how they multiply; and had identified or characterized some minor virus groups including the Mason-Pfizer Monkey Virus (MP-MV) and guinea pig endogenous virus.

4. Type C viruses: Again, by 1975 we had learned that Type C viruses generally fall into two classes, leukemia and sarcoma. Both were found in a wide variety of species in which they cause leukemias, lymphomas and related cancers. We learned that, although all leukemia viruses can infect, multiply, and mature independently, most mammalian sarcoma viruses were discovered to be defective in the sense that they can transform cells which they infect but cannot replicate except in the presence of a helper leukemia virus. On the other hand, the leukemia virus was seen to supply the function lacking in the sarcoma virus but did not itself have the ability to transform cells. We had learned that various type C viruses recombine readily and that RNA, or genetic code material, from one type of virus can be packaged in a coat of another type.

5. With type B viruses the most extensively studied was the Mouse Mammary Tumor Virus (MMTV) which causes breast cancer in mice. Tying down the characteristics of this virus were at first difficult. We couldn't grow enough of the virus without a system for large-scale cultivation in tissue cultures. We solved that; stepped up production; and learned that a hormone, dexamethasone, strongly stimulates viral replication. This was the first time that scientists saw a hormone stimulating, preferentially, the genetic transcription of a specific genetic messenger (RNA).

6. We learned that type C and type B viruses could either originate inside of a body or can be transmitted from one animal to

another by artificial infection. We found that most wild types of viruses found in natural animal populations are not of this variety, but seem to originate inside of the animal's own body. This means that these viruses can exist as an integral, inheritable component of the cell genome, or reproduction entity. The viral genome is normally present in the cell in an unexpressed state from which it can be activated spontaneously, or by a variety of artificial means.

You have heard testimony that many cattle test positive for leukemia virus, but don't develop cancer. Only those animals which are of certain families, and infected as well, develop cancer.

7. While neither of these types of viruses seemed contagious in the usual sense, experiments with cats showed that the virus could spread from animal to animal especially if the animals lived in crowded conditions. Gibbon ape leukemia virus also appears to be able to spread in laboratory colonies as does avian (fowl) myeloblastosis virus. We don't know the mechanisms of transfer of viruses between animals, but the rate of spread observed is extremely low and rare as compared to diseases normally described as contagious.

8. Endogenous, or apparently inherited viruses, have been recovered from cells of mice, rats, hamsters, cats, chickens, and baboons. When tissues from these creatures are cultured, even though the cells appear virus free, if the culture is continued through enough generations a yield of complete or partial expressions of type C viruses can be induced.

9. Viral DNA sequences related to those of RNA tumor viruses were demonstrated to exist in the normal cells of many species of vertebrates, including primates and humans. We came to accept the theory that viral genes can be found in all normal vertebrate cells. They probably have an important function in normal development. Hybridization experiments show that these ubiquitous viral sequences have probably become part of the animal genomes, or reproduction entities, many millions of years ago and have evolved with their host species during the course of evolution.

10. We learned that the presence of RNA tumor virus in an animal does not necessarily lead to the development of malignant disease. It became apparent that several host genes affecting viral function could be identified and we could locate them in chromosomes. We are seeking better knowledge of the mechanisms of interaction. Tools are becoming more sensitive. We know that viruses can lose the ability to cause malignant transformation by mutation, for instance, but the biochemical nature of the transforming principle is still under investigation.

11. It was found that many of the known animal viruses grow well in human cells and can also transform them. There is always the problem of eliminating animal virus contamination in human cells to concentrate on those viruses or particles which are associated with human cancers. But there is no clear-cut test for "humaneness." Any human virus could be expected to be closely related to primate viruses and distantly related to other mammalian viruses. Hence we are exploring such questions as how much of a virus has to be human to call it human. Defective viruses are known which can only form complete viral particles with the help of other viruses. The final particle of a defective virus can contain components belonging to its helper virus and could, therefore, give misleading results when tests for its origin are conducted.

12. In the normal human cell, the viral DNA sequences appear to be largely repressed. If they have anything to do with cancer they should become activated when the cell undergoes transformation to the malignant state. The malignant cell should, therefore, contain appreciable amounts of typical products of RNA virus genes: RNA and protein molecules similar to those of the virus as well as the viral enzyme RDDP. Experiments to look for these components in human tumor cells have been done and positive results have been obtained in some cases. Normal human milk and cells from malignant human breast tumors contain biochemically defined "particles" that contain elements of identified viruses. In human milk, a few particles that look like type B RNA viruses have also been seen under

electron microscopes. The RNA of milk particles has sequence relationship to the RNA of breast cancer cells and the RNA found in breast cancer cells, in turn, has sequence homology to the RNA of types of mouse and monkey viruses.

These are just a few of the accomplishments of the first years of the National Cancer Institute's concentrated virus studies.

Along the way, the National Cancer Institute funds helped create the Western Hemisphere's only bovine leukemia center. About $7 million has paid for a unique, highly infected herd of dairy cattle which is maintained at the University of Pennsylvania as a national resource for studying new leads, new research ideas. This unit led the way in characterizing in 1972 the virus associated with bovine leukemia.

In 1979 a major symposium at Cold Spring Harbor, N.Y., drew virology scientists from sixteen nations. This latest large meeting on the subject has been summed up by one qualified observor as demonstrating that evidence still does not show a direct cause and effect relationship between viruses and human cancers. On the other hand, the frequent association of viruses with human cancers means that viruses should be considered a risk factor, that is,a factor which probably increases the risk of disease so that elimination of the factor might be a means of preventing or reducing the incidence of disease.

In other words, one of the questions addressed by your Committee has also recently been addressed by some of the leading cancer experts in the world. They share your concern. They share your perception of the need for more research.

I might say that, after I invited the outside group to criticize this concentrated virus program at the National Cancer Institute, both their criticisms and the National Cancer Institute's responses were intently scrutinized by both Houses' Appropriations Committees and that year the National Cancer Institute's funds were given a good percentage increase.

Mr. Chairman, thank you for letting me put these facts into the record.

CURRICULUM VITAE

Name: Frank Joseph Rauscher, Jr.

Date & Place of Birth: May 24, 1931, Hellertown, Pa.

Marital Status: Married, 5 children

Education:

B.S., Premedical Curriculum, Moravian College, Bethlehem, Pa., 1953
Ph.D., Rutgers, The State University, New Brunswick, N.J., June 1957

Chronology of Employment:

1953-1955 -- Research Fellow in Virology, Rutgers University Graduate School, New Brunswick, N.J.
1955-1957 -- Research Assistant in Virology, Rutgers University Graduate School, New Brunswick, N.J.
1957-1958 -- Research Associate in Virology, Rutgers University Graduate School, New Brunswick, N.J.
1958-1959 -- Assistant Professor of Virology, Rutgers University Graduate School, New Brunswick, N.J.
1959-1964 -- Microbiologist, National Cancer Institute, Laboratory of Viral Oncology
1962-1967 -- Visiting Investigator of Viral Oncology, Rutgers University
1959- Visiting Instructor of Animal Virology, Trinity College, Washington, D. C.
1964-1966 -- Head, Viral Oncology Section, Laboratory of Viral Oncology, National Cancer Institute
1964-1970 -- Chairman, Special Virus (Leukemia) Cancer Program, Etiology, NCI
1965-1966 -- Acting Chief, Viral Leukemia & Lymphoma Branch, Etiology, NCI
1966-1967 -- Chief, Viral Leukemia & Lymphoma Branch, Etiology, NCI
1967-1970 -- Associate Scientific Director for Viral Oncology Etiology, NCI
1969-1970 -- Acting Scientific Director for Etiology, NCI
1970-1972 -- Scientific Director for Etiology, NCI
1972-1976 -- Director, National Cancer Program, National Cancer Institute
Nov. 1976 -- Senior Vice President for Research, American Cancer Society

Societies:

The Theobald Smith Society, N.J.
Society of Sigma Xi
The American Association for Cancer Research
The American Association of Immunologists
The American Association for Advancement of Science
World Society for Leukemia & Related Diseases
American Society of Clinical Oncology, Honorary Member
The American Academy of Microbiology

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Honors & Other Special Scientific Recognition:

1. Honorary Visiting Investigator of Viral Oncology
Rutgers, The State University, New Brunswick, N.J.

2. Visiting Faculty Member, Trinity College
Washington, D. C. 1959--.

3. Recipient of Competitive Travel Award to attend International Cancer Congress, Moscow. 1962.

4. Comenius Award - Presented annually by Moravian College, Bethlehem, Pennsylvania, to a person "for outstanding scientific achievement." April 1963.

5. United States Junior Chamber of Commerce Award -- Presented to the Nation's "Ten Outstanding Young Men." January 1965.

6. Panel Member, Board of U.S. Civil Service Examiners. 1965--.

7. Selman A. Waksman Honorary Lectureship Award -- Presented annually by the Theobald Smith Society, the New Jersey Branch of the American Society for Microbiology for "Outstanding contributions to Microbiology." March 1967.

7a. Member, NCI Scientific Directorate, 1968.

8. Arthur S. Fleming Award -- Presented annually to the "Ten Outstanding Young Men in the Federal Government." February, 1968.

9. Vice President, World Society for Comparative Leukemia Research. 1967-1972.

10. Elected to Board of Directors, American Association for Cancer Research. 1970.

11. Member, Fellowship Advisory Board, National Academy of Sciences. 1970.

12. Program Chairman, Annual Meeting of the American Association for Cancer Research. For 1971.

13. Elected - Board of Trustees, in April 1970, of Moravian College, Bethlehem, Pennsylvania, for the period 1971-1974.

14. Member, Council on Analysis and Projections.
American Cancer Society. 1971-1974.

15. Invited to serve as chairman of 10 plenary or area sessions at annual scientific meetings of the American Association of Cancer Research, American Society of Hematology, World Society for Comparative Leukemia Research, et al.

Research Interests:

Scientific. -- Comparative host responses to the necrotizing (e.g., influenza) and to the tumorigenic (e.g., Rous Sarcoma and murine-leukemia) viruses, known tumor-virus-host model systems to the search for etiologic agents in human neoplasms.

Management. -- The planning, implementation, monitoring and coordination of broad international mission oriented programs to determine the causes of cancers and to develop effective means for the prevention of these diseases in man.

Principal Scientific & Management Activities:

(1) Demonstrated that many host responses to Rous sarcoma virus (RSV) are directly related and dependent on the infecting dose of virus. Showed further that host response to RSV may resemble or differ, depending on the infecting dose of virus, from diseases produced by the nontumorigenic (necrotizing) viruses.

(2) Clarified the mechanisms by which noninfective tumors can be produced in susceptible hosts by RSV. Showed that the infecting dose of virus, age of the tumor, virus-neutralizing factors in tumor extracts and sera, and, the anatomical portion of the tumor selected for assay are important synergistic factors influencing the infective titer of tumor tissue.

(3) Developed and quantitated methods for detecting and assaying sub-tumor-producing doses of virus in various host systems, and for increasing the susceptibility of the host to minute amounts of virus.

(4) Characterized the embryonated egg of Japanese quail and both conventional and germfree post-hatched Japanese quail as new, quantitatable host systems for studying viruses.

(5) Discovered and characterized a new murine leukemogenic virus and its induced disease. This virus produces an intense erythrocytopoiesis within 4 days and lymphoid leukemia at least as early at 12 days post inoculation in adult mice and rats of many strains. The extremely short latent period, high potency, and stability of the relatively pure plasma preparations of virus permit studies on its chemotherapy, and biological, physical, and chemical properties in one fourth of the time required with some other laboratory model systems of neoplasia. This virus has been supplied to over 800 different laboratories throughout the world, and is currently being used routinely in studying different aspects of viral neoplasia. Over 5,000 papers have been published on studies using this system.

ABSTRACTS

1. Rauscher, F. J., and Groupé, V.: Growth curve of Rous sarcoma virus (RSV) in chick brain. Fed. Proc. 16: March 1957.

2. Rauscher, F. J., and Groupé, V.: Further studies on noninfective tumors in turkeys produced by Rous Sarcoma virus. Proc. Amer. Ass. Cancer Res. 3: 55, 1959.

3. Rauscher, F. J.: A virus-induced disease of mice characterized by erythrocytopoiesis and lymphoid leukemia. Proc. Amer. Ass. Cancer Res. 3: 352, 1962.

4. Rauscher, F. J.: Growth curve of a murine leukemia virus in mice. Proc. Amer. Ass. Cancer Res. 4: 55, 1963.

5. Zeigel, R. F., Burmester, B. R., and Rauscher, F. J.: An electron microscopic study of the chick embryo pancreas following natural and artificial transmission of avian tumor viruses. Proc. Amer. Soc. Cell Biol., Nov. 1963.

6. Zeigel, R. F., and Rauscher, F. J.: Correlation of the effects of physiochemical forces on the morphology and biological activity of a murine leukemia virus (Rauscher). J. Applied Physics. EMSA Abst., 1963.

7. O'Conner, T. E., Rauscher, F. J., and Zeigel, R. F.: Fission of a murine leukemia virus (Rauscher). Proc. Amer. Ass. Cancer Res. 5: 48, 1964.

8. Rauscher, F. J.: Progress in the viral research of human leukemia. Proc. 3rd Int. Symp. Comp. Leukemia Res., Paris, 1967; Bibl. haemat., No. 31, Karger, Basel, New York, 1968.

STATEMENT OF DR. JACK E. WHITE, DIRECTOR, CANCER CENTER, HOWARD UNIVERSITY

Mr. Chairman, members of the subcommittee, I am not an expert on cancer in animals. However, I believe research on spontaneous animal cancers is important as a means of improving the quality of animal products. Certainly, any new knowledge of the basic mechanisms involved in the cellular changes discovered in research on animal populations will be useful in better understanding of cancer in man. Since my expertise is with human cancer, I shall now address that subject.

Investigators at the Howard University Cancer Center have done epidemiologic research which shows an ever increasing incidence of cancers in humans, especially among men, and particularly Black men. Most of the increase seems to be due to environmental causes.

The better understanding of the etiology and control of cancer continues to be the focus of intense basic and clinical research. Animal models have been used very effectively in elucidating answers to key question ssuch as, the role of viruses in the etiology of breast and cervical cancer, the importance of hormones in uterine, breast and prostatic cancers and mechanism of action of chemotherapeutic agents. Do hormones cause cancers, or are they by themsleves not initiators but rather alter the host environment so that other carcinogens are effective. The DMBA induced mammary tumor model (first reported by Charles Huggins) and the Dunning Rats model for transplantable prostatic carcinoma have been extremely useful in providing answers to the above mentioned quentions. Animal models, such as the mouse mammary tumor virus systems, have allowed one to question the role of viruses in the etiology of cancer and have been effectively used to answer the question whether cancer causing viruses can pass via placenta, milk or seminal fluids.

The development of prenioplastic lesion's into cancers is one of the challenging problems in oncology. Recent studies using animal models have provided the concept of a precursor stage (e.g., the hyperplastic alveolar nodule in breast cancer), which has a greater probability of developing into a mammary carcinoma than the normal epithelial cell of the breast tissue. A variety of etiological agents (viral, chemical, physical), can interact with both normal and prenioplastic stages to induce and promote tumorigenesis. This fact may be particularly important since many of the chemotherapeutic agents commonly used in breast cancer therapy are among those compounds which can enhance the rate of tumor formation from precursor lesions.

Similarly, important experimental data on tumor cell kinetics have been derived using animal tumor models and many important observations have been made. For example, metastases and small tumors appear to be highly proliferative compared to the primary tumor and larger tumors respectively. Tumors near blood vessels are more proliferative than those further away. Thus, it is apparent that to properly design a chemotherapeutic strategy for a single patient, cell kinetics data would be extremely useful information. Now that rapid *in vitro* techniques are becoming available, combination chemotherapy may soon become less empirical and much more rational.

The availability of athymic nude mice will also allow human tumors to be transplanted in such animals to determine the most effective and least toxic chemotherapeutic regimen for a particular cancer.

Thus tumor model systems in concert with experimental biology has provided an invaluable tool in our understanding of problems concerned with cancer etiology, tumor immunology, cell kinetics, tumor markers and experimental chemotherapy. As mentioned in this brief review, several observations have emerged that have had a clinical impact in the past and the use of these model systems will continue to provide useful data in the future, which will lead to more accurate diagnosis and subsequently improved treatment.

SPECIFIC ASPECTS OF RESEARCH AT HOWARD UNIVERSITY CANCER CENTER

Much of the activity, speculation and enthusiasm which was devoted to the study of informational macromolecules, such as DNA and RNA, has now swung towards problems of biologic membranes. This increased emphasis on the plasma membrane has occurred because it is now clear that many important biologic communications such as those between cells and their neighbors, or between cells and their environment, are transduced by macromolecules intimately associated with the cell membrane. In addition, many of the altered properties of malignant cells are thought to involve alterations in cell surface functions.

Several recent findings have made interferons of current special interest to oncologists. Through the persistent effort of Dr. Kari Cantell, Central Public Health Laboratory, Helsinki, Finland, and amount of human leukocyte interferon sufficient

for meaningful clinical studies of the effects of interferon on a few diseases has finally become available. Employing this interferon, a group at Stanford University, Stanford, California, under the direction of Dr. Thomas Merigan, has obtained evidence suggesting that human interferon may be useful in the treatment of chronic hepatitis B virus infection and has found that interferon treatment of herpes zoster complicating leukemias and lymphomas has led to more rapid resolution of lesions and prevention of systemic effects. In addition, preliminary results from the laboratory of Hans Strander (Karolinska Institutet, Stockholm, Sweden), who has been treating 28 osteogenic sarcoma patients with Cantell's human interferon, suggest that the group receiving interferon has a lower rate of metastasis than does a concurrent control group. Strander's studies, although not yet involving sufficient numbers of patients to be highly significant, appear to warrant serious consideration of human interferon as an antitumor agent: Animal studies supply strong evidence that in some situations interferons are effective in inhibiting tumor growth.

The Howard University Cancer Center has assembled a group of investigators to explore: (1) the reasons for the alterations and possible function of membrane macromolecules in malignant cells, and (2) the biochemical nature of the antiviral activity of interferon. These studies are being pursued in both tissue-culture and animal model systems by a group of biochemically oriented cell biologists, immunologists, endocrinologists, pharmacologists, virologists and geneticists.

Statement of Hon. Tom Loeffler, a Representative in Congress From the State of Texas

Mr. Chairman and Members of the Subcommittee, I appreciate the opportunity to present my views on legislation to promote animal cancer research. The importance of this legislation in demonstrating the strong commitment of the Congress to insure basic research on cancer in domestic animals, livestock, and wildlife, and the contribution which such research can make toward providing solutions to human cancers, cannot be overstated.

Losses in livestock and poultry caused by malignancies are of ongoing concern. During the last few years, American consumers have lost the availability of millions of pounds of federally inspected meat animals due to condemnations at the time of slaughter because of cancerous conditions. A conservative estimate of the direct economic losses associated with cancer in food producing animals and poultry totals nearly $26 million, resulting ultimately in higher prices to the consumer for these products.

Currently, there are two potential Federal sources of support to fund research on cancer problems in animals. The National Cancer Institute provides support only for research on animal cancer demonstrating either a potential human health hazard or a similar type of cancer in man. This severely limits animal cancer research, and does not address the problem of cancer in livestock and wildlife. However, research on cancer involving animals and poultry conducted by the Department of Agriculture through the Science and Education Administration has yielded many positive results, most notably in the area of neoplastic disease in poultry.

An expansion of SEA's role in animal cancer research should yield even more positive results, both in the area of cancer which is indigenous to animals and by providing an important and vital role in the total cancer research program. There is no doubt that increased knowledge and understanding of cancer in animals will provide valuable information for the study of cancer in man.

Mr. Chairman, this legislation will provide needed research in the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry, and wildlife, an effort which I strongly support. The bill is, I believe, necessary to protect the health of such animals, and, in turn, to insure greater productivity of our agricultural community in addition to the direct benefits to the cancer research effort.

As you are aware, the Science and Education Administration is presently spending about $8 million on cancer-related problems in domestic animals. S. 2043 would authorize greatly increased appropriations for this important program. While I firmly support the aims of this most critical legislation, I sincerely hope that appropriations action on the programs authorized by S. 2043 will also recognize the valuable contributions on other agriculture research performed by USDA during future appropriation considerations.

Again, I appreciate having the opportunity to present a statement to the Committee on this most important matter.

Thank you, Mr. Chairman.

STATEMENT OF ORVILLE SWEET, EXECUTIVE VICE PRESIDENT, NATIONAL PORK PRODUCERS COUNCIL

Mr. Chairman and members of the committee, we commend you and your subcommittee for holding this hearing on S. 2043. We also want to commend Senator Melcher for introducing this bill in the Senate. We believe Senator Melcher has spotlighted a neglected area of animal disease research, and therefore, this bill to authorize appropriations for cancer problems in domestic animals is timely and necessary.

We are not aware that cancer is a major problem in swine, although the records of the federal meat inspection indicates there were 3,331 swine condemned because of various neoplasia in 1978. This is not a large number, but undoubtedly many swine died before reaching inspection because of various neoplasia. Admittedly, this is not a serious swine disease.

We do not know of any evidence that any swine neoplasm is a hazard to human health. Therefore, our principal reason for supporting this bill is that we believe research in cancer of animals is certain to produce results which will be vital in attacking cancer in man. The similarity of man to lower animals is such that research conducted in animals will not only result in useful information to combat or prevent cancer in animals, but will also bring information and perhaps even breakthroughs in cancer research in man.

Swine may be the best animal model for man. Therefore, research on cancer in swine may be even more likely to produce lines of investigation that cannot be carried out in man, but may eventually prove important in solving a cancer mystery in man.

The National Pork Producers Council supports S. 2043 for all of the reasons mentioned above. We hope this subcommittee will act favorably on this bill and that it will pass the Congress. We believe that funds expended on animal cancer will be a good investment of government funds.

STATEMENT OF DR. GERALD J. DOMINGUE, PROFESSOR, DEPARTMENT OF UROLOGY AND DEPARTMENT OF MICROBIOLOGY & IMMUNOLOGY, TULANE UNIVERSITY, SCHOOL OF MEDICINE, NEW ORLEANS, LA.

I am testifying in support of Senator John S. Melcher's bill S. 2043 that provides for financial support for research on the diagnosis, prevention, and control of malignant tumors in domestic animals, poultry and wildlife.

I believe that there is compelling scientific evidence suggesting a role for bacteria and/or their products in malignant transformations. Of particular interest is the production of chorionic gonadotropin-like substance, a human hormone, (hereafter referred to as CG) by bacteria associated with malignancies. Additionally, it has been demonstrated that the surface of all cancer cells thus far tested show the presence of this hormone. This hormone therefore appears to be a common biochemical characteristic for cancer cells of all types, suggesting that cancer may be one disease. Because CG has a strong negative electric charge, it might very well defeat the human immunological system and enable cancer cells to invade and metastasize. Since cancer-related bacteria synthesize CG, development of a practical preventive vaccine against CG using cancer related bacteria that produce this hormone might be useful. This can only come about if research funds are made available for investigation in that direction.

Unfortunately, the role of bacteria in the etiology of cancer has been ignored by granting agencies (although they have been suspected of being causative agents of cancer for years) and as a result, a number of applications directed towards delineating the role of bacteria in cancer have not been funded. Senator Melcher's bill would provide an avenue for research support in this area.

I have been investigating for the past ten years, the role of cell-wall defective bacterial forms in kidney diseases and have found novel bacterial variants to be present in the blood cells of diseased and normal humans. We have demonstrated that human blood cells are parasitized with minimal reproductive units of bacteria that can be readily demonstrated in the blood of patients with nephritis and in urine containing blood cells from patients with idiopathic hematuria. Lately, we have found similar organisms in the blood of cancer patients. Lysis of erythrocytes with release of adsorbed bacteria is possibly responsible for such growth. Positive cultures were obtained more frequently and within a relatively short period, by using a rich variant medium and lysing the flood with hypotonic saline solutions

beforehand. The results were not altered when the lysates were filtered through a 0.22 micron filter. This filterability suggests that they are as small as certain viruses. It further connotes that organisms adsorbed on the erythrocytes are in an elemental form and that some of them have the essential biochemical machinery to revert to the parent organism if nutrients and cultural conditions are optimal. Convincing circumstantial evidence that points to a possible etiologic role for these unusual organisms and/or their products in disease has been obtained. Of particular significance, is the finding that some of the bacterial isolates obtained from patients with nephritis, and from fevers of unknown origin produce a human CG-like protein, as demonstrated by direct and indirect immunofluorescent studies with CG antiserum. There is no clinical evidence to indicate that these patients also have cancer. Therefore, it is of interest that CG-producing bacteria can be isolated from non-cancer patients, and such findings may suggest that CG-producing bacteria may also play a role in diseases other than cancer, or that the patients may have a malignancy that may not be clinically apparent. Since it has been shown that every cancer cell so far tested has CG in its membrane, it is important to determine if there is any link between CG-producing bacteria isolated from cancer patients and CG present in cancer cells.

In addition to over 500 humans studied, we have also performed preliminary experiments on the blood of rhesus monkeys, rabbits, mice, rats and sheep and have found these aberrant bacterial forms to be present. It is possible that humans and certain animal species may be universally infected with such organisms. We might live in harmony with these microbes until environmental and/or human factors trigger the organisms to change their phase and develop into disease producing agents, thereby becoming fulminant invaders that over-power human cells. These bacteria and/or their toxic materials could conceivably produce malignant transformations (cancer). Because of the possible link of these microbes with malignant transformations, investigations are urgently needed to determine whether bacteria present in various animal species related and unrelated to human disease and bacteria found in nature produce CG-like hormone. The scientific demonstration that there exists a CG biological association among cancer cells, trophoplasts and bacteria isolated from cancer patients and patients with kidney diseases, expose the potential for a specific immunological approach to the prevention and treatment of disease as well as for fertility control. I feel certain that you would agree that cancer is an important disease to conquer and that innovative research approaches should be fully explored if we are to continue to attempt to prevent the yearly death of an estimated 400,000 cancer patients. Obviously, if a vaccine were developed, and proved to be effective, this might provide the best approach for eradication of the disease.

Experimental animals, compromised and non-compromised should be injected with CG-producing bacteria isolated from cancer patients and cancerous animals to determine whether tumors develop in normal animals so infected along with appropriate controls of animals injected with non-CG-producing organisms. Additionally, protective studies with antisera to CG for determining whether such antibodies prevent the development and spread of malignancies should be under taken. It would be worthwhile to expose malignant cells *in vitro* to antisera derived from CG-producing bacterial vaccines and from human CG vaccines prior to injection into animals to determine whether there is a protective effect from development of cancer in the animals. Animals should be immunized with vaccines containing CG-producing bacteria and with human CG prior to injection of malignant cells to determine whether immunized animals will be protected from the development of a malignancy in comparison to non-immunized animals. These are but a few of the experiments that I feel are importunately needed to determine the role of CG-producing bacteria in malignancies. Furthermore, it should be possible to determine using cell-wall deficient variants of these CG-producing bacteria whether these organisms have the capability of converting normal cells to malignant cells in a tissue culture system. It is necessary to determine by all currently available scientific methods whether there is any link between CG-producing bacteria isolated from cancerous humans and animals and CG present in cancer cells. There is no question but that logical scientific approaches to the problem are hastily needed. Well-designed and well-controlled experiments should be initiated to determine the biological significance of CG-producing bacteria in cancer and other allied diseases. Data obtained from such investigations would very likely help to clarify this intriguing biological phenonenon and would and would hopefully benefit mankind.

I fully realize that this is a very controversial area of research. I would like to close by quoting a passage from Eric Hoffer in the *True Believer,* for I believe that it is quite apropos to this disputatious scientific issue.

"A depreciating attitude toward the present fosters a capacity for prognostication. The well-adjusted make poor prophets. On the other hand, those who are at war with the present have an eye for the seeds of change and the potentialities of small beginnings. A pleasant existence blinds us to the possibilities of drastic change. We cling to what we call our common sense, our practical point of view. Actually, these are but names for an all absorbing familiarity with things as they are. The tangibility of a pleasant and secure existence is such that it makes other realities, however imminent seem vague and visionary. Thus it happens that when the times become unhinged, it is the practical people who are caught unaware and are made to look like visionaries who cling to things that do not exist. On the other hand, those who reject the present and fix their eyes and hearts on things to come have a faculty for detecting the embryo of future danger or advantage in the ripeness of their times. Hence the frustrated individual and the true believer make better prognosticators than those who have reason to want the preservation of the status quo. 'It is often the [reactionaries] and not always the delicate spirits, that are found grasping the right thread of the solutions required by the future.' "

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